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The impact of age on physical functioning after treatment for breast cancer, as measured by patient-reported outcome measures: A systematic review

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ABSTRACT

Purpose: This systematic review aims to explore the impact of age on physical functioning post-treatment for early-stage, locally advanced, or locally recurrent breast cancer, as measured by patient-reported outcome measures (PROMs), identify PROMs used and variations in physical functioning terms/labels.
Methods: MEDLINE, EmBase, PsycINFO, CINAHL and AMED were searched, along with relevant key journals and reference lists. Risk of bias (quality) assessment was conducted using a Critical Appraisal Skills Programme checklist. Data was synthesised through tables and narrative.
Results: 28,207 titles were extracted from electronic databases, resulting in 44 studies with age sub-groups, and 120 without age sub-groups. Of those with findings on the impact of age, there was variability in the way findings were reported and 21 % found that age did not have a significant impact. However, 66 % of the studies found that with older age, physical functioning declined post-treatment. Comorbidities were associated with physical functioning declines. However, findings from sub-groups (breast cancer stage, treatment type and time post-treatment) lacked concordance. Twenty-eight types of PROM were used: the EORTC QLQ-C30 was most common (50.6 %), followed by the SF-36 (32.3 %). There were 145 terms/labels for physical functioning: 'physical functioning/function' was used most often (82.3 %).
Conclusions: Findings point towards an older age and comorbidities being associated with more physical functioning declines. However, it was not possible to determine if stage, treatment type and time since treatment had any influence. More consistent use of the terminology 'physical functioning/function' would aid future comparisons of study results.

1. Introduction

Survival rates for early-stage breast cancer are improving [1–4,5,6], with increased screening [2,3,7,5] and treatment advances [2,7,5]. Despite the recognised importance of addressing lasting symptoms and side-effects requiring multidisciplinary support post-breast cancer treatment [7,5,8], follow-up care tends to focus on identifying relapse [7]. Recent literature has recognised the importance of developing knowledge on physical functioning post-breast cancer treatment [9] and increasing the awareness of the importance of monitoring and addressing physical functioning declines [10]. The population is ageing [4,11] and previous research has found that amongst breast cancer survivors, physical functioning declines are exacerbated with increasing age [12,13,8,14,15,16]. There is a lack of clarity on what physical functioning encompasses [17,18,19]. Definitions include different physical aspects [20,18,19]. Stewart and Kamberg's (1992) definition was used for this systematic review: "the performance of or the capacity to perform a variety of physical activities normal for people in good health. Such physical activities include bathing, dressing, walking, bending, climbing stairs, and running" [13, p.86].

Alongside being essential for functioning independently [21,22,23,24,25,26], physical functioning limitations can have a negative impact

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on quality of life (QoL) [27,23,24,25], further burdens on caregivers [22] and is associated with an increased risk of mortality amongst cancer survivors [28,29]. It is possible that older patients may be undertreated, as medical professionals can be reluctant to prescribe chemotherapy for older patients due to factors including deteriorations in functioning and comorbidities [30–33]. Therefore, enhanced knowledge on physical functioning amongst older patients post-treatment is particularly important to help inform clinical decision making.

Patient-reported outcome measures (PROMs) are becoming more widely used in health care to assess and monitor symptoms, treatment side-effects and QoL [34,21,35,36–39] and enhance patient-centred care and communication between patients and health professionals [35,37,39,40]. Patient-reported outcomes (PROs) have been defined as a "report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" [41, p.2]. PROMs can be completed on paper, over the telephone, or electronically, and therefore can be completed at appointments or remotely [36–40]. Although physical functioning can also be assessed by objective measures such as tracking devices, PROMs are widely used to measure physical functioning.

There is a need for a systematic review exploring the impact of age on physical functioning after treatment for early-stage, locally advanced, or locally recurrent breast cancer, as measured by PROMs (primary review question). The PROMs used and variations in language to refer to the term/label 'physical functioning' also need to be addressed to provide conceptual and methodological clarity (secondary review questions) [20,18].

2. Methods

The systematic review methods are published on PROSPERO [42].

2.1. Inclusion criteria

1. Participants aged 16 years of age or over after treatment for early-stage, locally advanced, or locally recurrent breast cancer [43]. Participants may still be on hormone treatment but have completed one or more other form of treatment, which could be surgery, radiotherapy, chemotherapy, or targeted therapy [44–46].
2. Studies using a PROM for physical functioning according to Stewart and Kamberg's (1992) definition of physical functioning [47], and that state the physical functioning findings of the PROM
3. Quantitative research
4. Literature in English language
5. Research on humans
6. Non-pharmacological studies
7. Primary or secondary research
8. Literature from the last 15 years

2.2. Exclusion criteria

1. Studies on metastatic breast cancer, or including early-stage, locally advanced, or locally recurrent and metastatic breast cancer, that do not report the physical functioning findings for participants with early-stage, locally advanced, or locally recurrent breast cancer separately [43,44].
2. Studies where PROMs only focus on measurements of exercise, such as the Godin-Shephard Leisure-Time Physical Activity Questionnaire [48], and symptoms rather than physical functioning, such as Functional Assessment of Cancer Therapy measures [49].
3. Studies including a mix of cancer types that do not report the findings separately for breast cancer
4. Outcome measures completed by clinicians
5. Objective measures
6. Studies for which the full-text is not available
7. Studies involving interventions other than treatment for breast cancer, where the intervention could impact on physical functioning, such as mindfulness-based stress reduction, or physical exercise

2.3. Search strategy

The following electronic databases were searched: MEDLINE, EmBase, PsycINFO, CINAHL and AMED. Search terms were a combination of terms and subject headings involving aspects encompassed by physical functioning, breast cancer, and after treatment (Appendix A). These were combined with the Boolean terms "AND" and "OR". Search terms were developed on MEDLINE and adapted to the other databases. Reference lists of relevant studies with age sub-groups were reviewed for further literature and key journals searched.

The literature screening process was documented in accordance with the PRISMA (2009) flow diagram [50]. The primary researcher (VR) conducted all literature screening, with two other researchers (SG and KA) each screening a random 10 % selection of titles, abstracts, and full-texts to ensure reasonable concordance. References and data were managed using EndNote (Version X9.3.3) and Microsoft Excel. The search was updated prior to commencing the data synthesis to ensure findings are up to date.

2.4. Data extraction

Data was extracted on Microsoft Excel using two separate files: one containing literature with age sub-groups (addressing the primary and secondary review questions), and one without age sub-groups (addressing the secondary review questions). Data extracted from literature with age sub-groups included: the country, study design, participant information (number, age, breast cancer stage, treatment, and time since diagnosis/treatment), physical functioning PROMs and terms/labels, and physical functioning findings (for age sub-groups and additional sub-groups). Data extracted from literature without age sub-groups included: the age of participants, and physical functioning PROMs and terms/labels.

The primary researcher extracted all data. Two other researchers (SG and KA) also extracted data for a total of a random 20 % selection of the full-texts with age sub-groups, and 10 % without age sub-groups. Any variations in data extracted were explored and discussed.

2.5. Risk of bias (quality) assessment

The Critical Appraisal Skills Programme (CASP) cohort study checklist was completed for each study with age sub-groups [51]. This assesses the validity, findings and applications of findings [51]. Scores were assigned to each of the 12 tick box questions with responses "Yes" = 2, "Can't tell" = 1 and "No" = 0. Range of scores (maximum score = 24, minimum score = zero). The assessment was conducted by the primary researcher with one other researcher (SG) assessing a random selection of five (11.4 %) studies. Discussions on variations in assessments involved a third researcher (KA), and answers were revisited and revised where relevant.

2.6. Data synthesis

Due to the multifaceted aspects of the concept being researched, and the variety of PROMs used and methods of analysis, meta-analysis was not possible. Data was synthesised through tables and narrative using Campbell et al.'s (2020) guidance [52]. Tables were ordered by physical functioning PROMs, then risk of bias (quality). Findings were considered statistically significant if $p < 0.05$. Within the literature with age sub-groups, additional sub-groups were considered for inclusion if the sub-groups were relevant and included by several studies.

3. Results

3.1. Study selection

28,207 titles were extracted from the electronic databases (Fig. 1), and after inclusion/exclusion criteria were applied and relevant key journals and reference lists searched, 44 relevant studies with age sub-groups were included (Table 1), and 120 without age sub-groups.

3.2. Studies with age sub-groups

3.2.1. Study information

Nineteen studies (43.2 %) were conducted in America, 18 (40.9 %) Europe, six (13.6 %) Asia, and one (2.3 %) Africa (Table 1). Most were observational, cross-sectional, cohort, or case-control studies (n = 39, 88.6 %), although five (11.4 %) were randomised controlled trials. Studies included a wide range of numbers of participants, with the minimum being 48 participants [53,91] and maximum 6,949 [71] (Table 1). Most studies (n = 30, 68.2 %) included participants of a range of ages. However, 12 studies (27.3 %) included only participants aged 65 years or over, and two (4.5 %), participants aged 64 or under

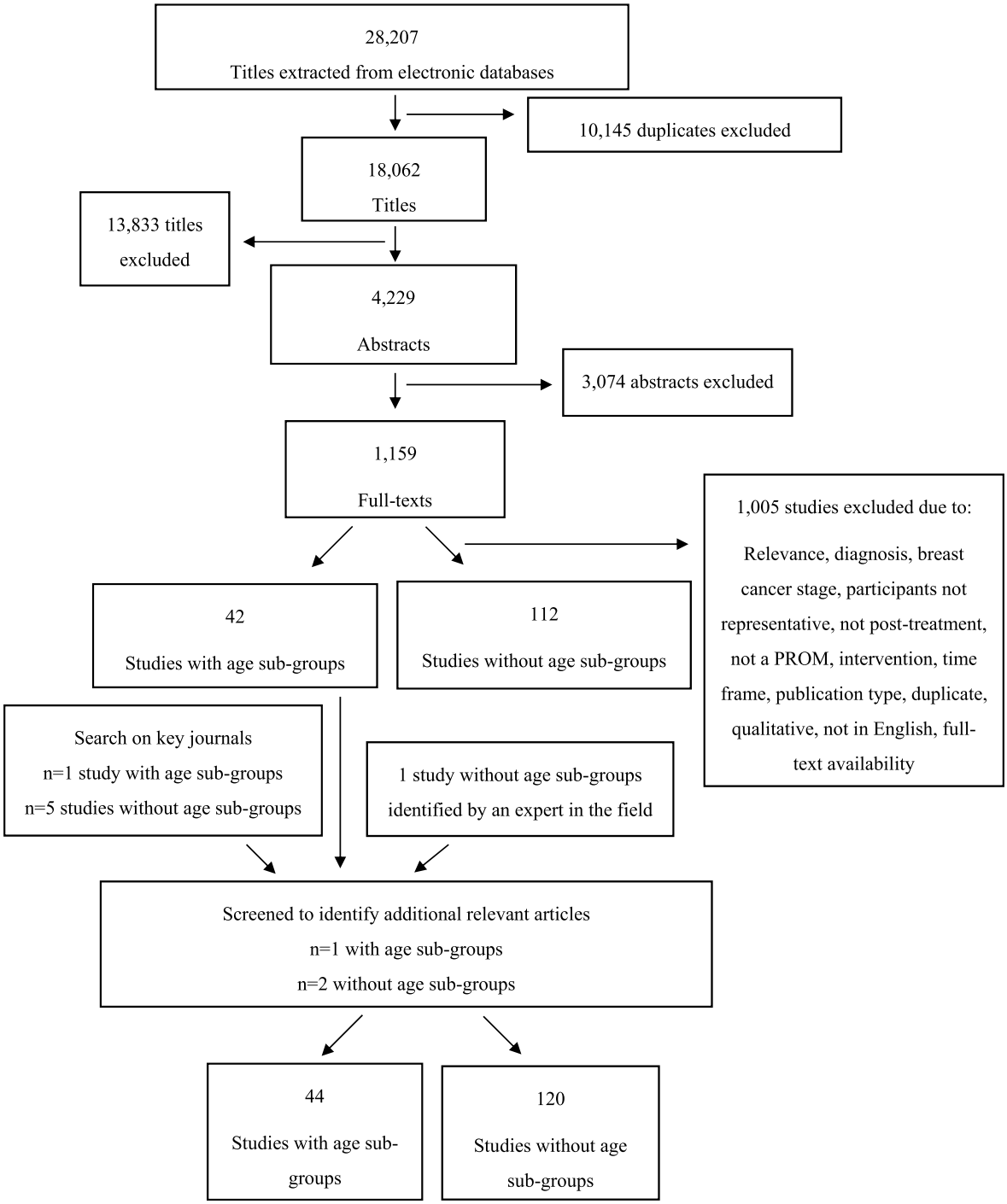

Fig. 1. Diagram of systematic review screening process, adapted from the PRISMA (2009) flow diagram [50].

Table 1
Study information, PROMs used, and key findings of studies with age sub-groups.

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
Arraras et al. (2008) [53]	Spain	48	65–87	EORTC QLQ-C30[a]	Mean (SD[a]): baseline: 94.8 (12.8), final day of radiotherapy: 88.5 (16.8), 6 weeks post-radiotherapy: 93.7 (11.2). A significant worsening was found for the final day of radiotherapy, improvement post-treatment, but not significant improvement compared to baseline physical functioning (although p-value not stated and $p < 00.001$ considered statistically significant rather than $p < 00.05$).
Arraras et al. (2016) [54]	Spain	243	34–68	EORTC QLQ-C30[a]	Mean (SD[a]), 88.2 (15.1). The impact of age on physical functioning was not studied, but 231 participants (95.1 %) were aged ≤65 years and only 12 participants (4.9 %) were aged 66–68 years.
Arraras et al. (2016) [55]	Spain	173	≥65	EORTC QLQ-C30[a]	Mean. Baseline physical functioning: 84.6, final day of radiotherapy: 81.8, 6 weeks post-radiotherapy: 85.6. 6 weeks post-radiotherapy vs. baseline not significant (0.375), global time ($p = 0.001$). EORTC QLQ-C30 ALND[a] baseline 79.5, final day of radiotherapy 77.1, 6 weeks post-radiotherapy 80.6; SLNB[a] baseline 87.6, final day of radiotherapy 85.1, 6 weeks post-radiotherapy 88.7; No surgery baseline 86.0, final day of radiotherapy 83.5, 6 weeks post-radiotherapy 87.1 (time p-value = 0.005).
Battisti et al. (2021) [56]	UK	3,416	≥69	EORTC QLQ-C30[a], EQ-5D-5L[a]	The impact of chemotherapy vs. no chemotherapy was significant at 6 months (medium difference: 8.05, CI[a]: 10.21 to −5.89, $p < 0.001$) and 12 months (small difference: 2.76, CI[a] −4.95 to −0.57, $p = 0.014$), but not 6 weeks, 18 months or 24 months. The impact of chemotherapy on EQ-5D-5L mobility improved at 6 months. EORTC QLQ-C30 physical functioning mean (SD[a]), chemotherapy: baseline 87.1 (16.0), 6 weeks 79.3 (18.8), 6 months 71.8 (20.5), 12 months 76.9 (19.5), 18 months 75.6 (20.9); no chemotherapy: baseline 82.1 (19.9), 6 weeks 76.2 (19.9), 6 months 75.7 (20.5), 12 months 74.9 (21.6), 18 months 74.1 (21.0).
Blackwood et al. (2020) [57]	USA	Stage 2 breast cancer (local): n = 963, Stage 3 breast cancer (regional): n = 355	≥65	Katz's ADL[a] Index	Stage 2: difficulties in continence (n = 489, 49.0 %), transfers (n = 4250, 24.9 %), bathing (n = 169, 16.8 %), dressing (n = 116, 11.5 %), toileting (n = 90, 9.0 %), and feeding (n = 44, 4.4 %). Stage 3: difficulties in continence (n = 176, 47.7 %), transfers (n = 107, 29.4 %), bathing (n = 76, 21.1 %), dressing (n = 52, 14.1 %), toileting (n = 43, 11.6 %), and feeding (n = 30, 8.1 %).
Braithwaite et al. (2010) [58]	USA	2,202	21–79	Ability to perform daily activities in the past month. Taken from Framingham Disability Study, Established Populations for Epidemiologic Studies of the Elderly, and Nagi, Rosow and Breslau's measures	The proportion of physical functioning limitations generally increased with age ($p < 0.001$). Amongst participants aged 65–79 years, 39.2 % had at least one physical functioning limitation, and 23.8 % did not have physical functioning limitations. Amongst participants aged <50 years, 17.9 % had physical functioning limitations and 29.0 % did not. In the 50–64 age group, 42.9 % had physical functioning limitations and 47.2 % did not.
Brandberg et al. (2020) [59]	Sweden	760	18–65	EORTC QLQ-C30[a]	Post-surgery, prior to chemotherapy. Mean (SD[a]): 90.5 (11.4), 89.5 (13.4). At end of chemotherapy: Mean (SD[a]): tailored chemotherapy group; 64.9 (21.5),

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Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
					standard chemotherapy group: 73.6 (18.9). Mean difference (99 % CI[a]) −9 (−12 to −6), $p < 0.001$. At first follow-up visit (4 months): Mean (SD[a]): tailored chemotherapy group; 82.2 (16.6), standard chemotherapy group: 84.4 (14.6). Mean difference (99 % CI[a] −3 (-6 - 1), $p = 0.031$. Test for interaction $p < 0.001$.
Browall et al. (2008) [60]	Sweden	75	55–77	EORTC QLQ-C30[a]	Mean (SD[a]). Participants aged 55–64: baseline 92 (8), 4 months post-treatment 82 (14). Participants aged 65–77: baseline 87 (17), 4 months post-treatment 79 (19). Significant time effect regardless of age $p < 0.001$.
Browall et al. (2013) [61]	Sweden	102	55–80	SF-36[a]	A decrease-stable pattern, demonstrated by a significant deterioration from baseline to 1 week post-chemotherapy or 2 weeks post-radiotherapy but no significant change between 1 week post-chemotherapy or 2 weeks post-radiotherapy and 5 years post-treatment. Baseline – mean (SD[a]), participants: 88.6 (16.9), normative sample: 72.9 (24.9), *t*-test 7.28, $p = 0.00$, Cohen's $d = 0.63$. 5 years post-treatment – mean (SD[a]), participants: 78.7 (20.5), normative sample: 67.8 (27.0), *t*-test 3.81, $p = 0.00$, Cohen's $d = 0.40$. Over time ($n = 96$), mean (SD[a]), baseline 90.5 (13.9), 1 week post-chemotherapy or 2 weeks post-radiotherapy 77.2 (20.3), 5 years post-treatment 78.1 (20.5), $F = 32.6$, $p = 0.00$, partial eta-squared effect size = 0.26.
Champion et al. (2014) [62]	USA	182	≤78	SF-36[a]	Adjusted mean (SE[a]): age ≤53 years; 81.9 (0.81), age 58–78 years 80.8 (0.88), p-value = 00.605 (0.626). Younger control group 83.3 (1.05). Younger control group vs. participants age ≤53 years; F test (p-value): 0.482 (0.540). Post-menopausal participants had significantly worse physical functioning: mean (SD[a]): pre-menopausal; 89.6 (16.3), post-menopausal; 77.9 (22.7) ($p < 00.0001$).
Clough-Gorr et al. (2010) [63]	USA	660	≥65	SF-36[a]	1 or more physical functioning limitation: 37 %
Cohen et al. (2012) [12]	USA	153	40 - 86. $n = 79 < 65$, $n = 74 \geq 65$	EORTC QLQ-C30[a]	After controlling for comorbidities or symptoms, age still had a significant relationship with physical functioning ($p < 0.01$) (older age was associated with physical functioning declines). Of the different aspects of physical functioning, patients aged ≥65 were significantly more likely to have struggles only with taking a long walk ($p < 00.001$). Physical functioning of participants aged ≥70 is 71.2, not significantly different to the general population (67.7) ($p = 0.427$).
de Ligt et al. (2019) [64]	The Netherlands	876	27.5–91.6	EORTC QLQ-C30[a]	Physical functioning was significantly better (5 points difference) in the general population when compared to participants with breast cancer diagnoses aged <50 years. Older age was significantly associated with lower physical functioning (age 60–69: β: −6.8, $p = 0.002$; age ≥70: β: −13.5, $p < 0.001$). Comorbidities were negatively associated with physical functioning (β: −6.1, $p < 0.001$).
Dialla et al. (2015) [65]	France	396	27–96	SF-12[a]. EORTC QLQ-C30[a]	With SF-12[a], participants aged <65 years had a significantly better physical functioning, mean (SD[a]), median (minimum-maximum): 74.6 (27.3), 75.0 (0–100) than participants aged ≥65 years: 55.3 (33.8), 50.0 (0–100) ($p < 0.001$).

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Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
					With EORTC QLQ-C30[a], participants aged <65 years had a significantly better physical functioning, mean (SD[a]), median (minimum - maximum): 84.2 (16.1), 86.7 (20–100) than participants aged ≥65 years: 84.2 (16.1), 86.7 (20–100) ($p < 0.001$). The multivariate analysis found that participants aged ≥65 years had a significantly worse physical functioning.
Dubashi et al. (2010) [66]	India	51	≤35	EORTC QLQ-C30[a]	Physical functioning mean (SD[a]): 86.39 (17.56). MRM[a] 87.81 (17.32), BCS[a] 83.77 (18.18) ($p = 0.43$).
Enien et al. (2018) [67]	Egypt	172	<40 n = 47, 40–50 n = 75, >50 n = 50	EORTC QLQ-C30[a]	Physical functioning was correlated with age ($p = 0.001$); participants aged <40 years tended to have a better physical functioning.
Extermann et al. (2017) [68]	USA	56	≥65	SF-36[a]	Mean (SD[a]). Physical functioning was slightly but not significantly lower after adjuvant chemotherapy: 58.0 (34.2), compared to no adjuvant chemotherapy 72.2 (23.8) ($p = 0.07$).
Girones et al. (2010) [69]	Valencia	91	≥70	Katz's ADL[a] Index	Age had a statistically significant correlation with physical functioning: more physical functioning limitations with increasing age ($p < 0.0001$). ADL[a] dependencies: 0–76 %, 1–2 %, 2–3 %, 3–8 %, 4–7 %, 5 - 4 %. Small percentage of participants with physical functioning limitations (only 4 % fully dependent). Participants required assistance in: 23 % continence, 22 % using the bathroom, 17 % ambulation, 11 % dressing, and 8 % eating.
Jayasinghe et al. (2021) [70]	Sri Lanka	54	36 - 81. ≤ 60 n = 33, >60 n = 21	EORTC QLQ-C30[a]	The physical functioning scores for participants aged ≤60 years was not significantly different to the participants >60 ($p = 0.531$). Physical functioning for participants aged ≤60 years median: 73.33, range: 33.3–100. For participants aged >60 years, median: 73.3, range: 41.7–100.
Jones et al. (2015) [71]	USA	6,949	≥50	SF-36[a]	Age had a significant association with physical functioning ($p < 0.01$). Older age was associated with physical functioning declines: for each year of age, physical functioning deteriorated by 0.58 points, and for every 10 years of age, physical functioning deteriorated by 5.80 points (range 0–100).
Kamińska et al. (2015) [72]	Poland	85 after breast conserving therapy, 94 after mastectomy	30–70	EORTC QLQ-C30[a]	Two age groups: 30–45 years of age and 45–70 years of age: no significant difference on physical functioning for BCS or mastectomy group. The best physical functioning was by patients after BCS.
Karlsen et al. (2016) [73]	Denmark	542	Baseline 50.3–65.2, First follow-up 54.4–70.8, second follow-up 63.8–80.9	SF-36[a]	Mean difference between first and second follow-up (95 % CI[a]), physical functioning, participants aged ≤60 years −1.2 (−3.9 to −1.4), >60 years −2.6 (−4.9 to −0.3) (this is significant for the participants >60 years, although the level of significance is not stated).
Klein et al. (2011) [74]	France	652	Wide range. ≤ 54 n = 127, ≥55 n = 525	SF-36[a], EORTC QLQ-C30[a]	SF-36[a]: Physical functioning scores were higher amongst younger participants. Values are approximate as taken from a bar chart, but participants aged ≤54 years: 5 years post-diagnosis 72, 10 years post-diagnosis 82, 15 years post-diagnosis 84, healthy control group 87. Participants aged 55–64 years: 5 years after diagnosis 71, 10 years after diagnosis 76, 15 years after diagnosis 86, healthy control group 81. Participants aged 65–74 years: 5 years after diagnosis 67, 10 years after diagnosis 68, 15 years after diagnosis 71, healthy

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Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
					control group 72. Participants aged ≥75 years: 5 years after diagnosis 42, 10 years after diagnosis 52, 15 years after diagnosis 57, healthy control group 53.
Kornblith et al. (2011) [75]	USA	350	≥65	EORTC QLQ-C30[a]	After adjustment for potential confounders in a linear mixed-effects model, physical functioning mean (SE[a]), baseline, mid-treatment, end of treatment, 12 months, 18 months, 24 months: standard chemotherapy (CMF[a] or AC[a]): 86.3 (1.3), 76.6 (1.4), 74.5 (1.3), 82.0 (1.4), 81.4 (1.4), 80.8 (1.4); capecitabine: 84.4 (1.4), 78.4 (1.4), 79.1 (1.4), 79.9 (1.5), 80.9 (1.5), 79.1 (1.5). The p-value between the two types of chemotherapy at the end of treatment at p = 000.019 - this is the only time point that is significant. After adjustment for potential confounders in observed mean scores, t-tests, physical functioning mean (SE[a]), baseline, mid-treatment, end of treatment, 12 months, 18 months, 24 months: standard chemotherapy (CMF[a] or AC[a]): 86.2 (1.3), 77.0 (1.6), 74.9 (1.6), 82.1 (1.5), 81.3 (1.6), 80.3 (1.6); capecitabine: 84.2 (1.3), 78.8 (1.7), 79.8 (1.5), 80.5 (1.7), 81.2 (1.7), 80.5 (2.0). The p-value between the two types of chemotherapy at the end of treatment at p = 000.027 - this is the only time point that is significant.
Kostic et al. (2020) [76]	Serbia	170	n = 43 < 50, n = 127 ≥ 50	EORTC QLQ-C30[a]	Mean (SD[a]): physical functioning pre-surgery <50 years 90.3 (11.4), ≥50 years 83.7 (18.8) (p = 0.103) (not significant). Post-surgery age differences also not significant, <50 years 81.2 (16.7), ≥50 years 76.5 (18.7) (p = 0.134). Within <50 year age group difference pre-to post-surgery significant (p=<0.001). Within ≥50 year age group difference pre-to post-surgery significant (p=<0.001).
Leinert et al. (2017) [77]	Germany	1,363, 218 age 65–70, 1,145 < 65 years	18–70	EORTC QLQ-C30[a]	Physical functioning decreased from baseline until 4 weeks after chemotherapy by 13.4 points in patients aged ≤64 years, and by 15.9 points in patients aged 65–70 years (medium decreases). Greater difference in physical functioning between the groups when compared to the other QLQ-C30 scales, but still a small difference. Mean (95 % CI[a]) 4 weeks after chemotherapy 64.4 (59.8–69.0) in patients aged 65–70 years vs. 70.7 (68.9–72.5) in patients aged ≤64 years, and no significant difference between the age groups at any time point. In both age groups, physical functioning stayed under baseline 6 weeks after radiotherapy by 2–3 points, but started to reach baseline levels when compared to 4 weeks after chemotherapy (although a statistical test was not performed analysing this data). Mean (95 % CI[a]): baseline (before treatment): age 18–64: 84.1 (82.8–85.4); age 65–70: 80.3 (77.1–83.5) (not a significant difference). 4 weeks after chemotherapy: age 18–64: 70.7 (68.9–72.5); age 65–70: 64.4 (59.8–69.0) (small difference (6.3) that is not significant). 6 weeks after radiotherapy: age 18–64: 82.8 (80.5–85.1); age 65–70: 77.3 (71.7–82.9) (small difference (5.5) that is not significant). Significant increases between the point 4 weeks after chemotherapy compared to 6 weeks after radiotherapy: age 18–64: medium

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Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
					increase (12.1); age 65–70 - medium increase (12.9).
Lemieux et al. (2018) [78]	Canada	1,918	43–92.2	SF-36[a]	There were deteriorations in physical functioning with increasing age.
Maharjan et al. (2018) [79]	Nepal	107	n = 59 < 48, n = 48 > 49	EORTC QLQ-C30[a]	Median score (range): <48 years 86.66 (100–86.66), >49 years 86.66 (93.33–86.66), p-value = 0.066.
Mandelblatt et al. (2013) [80]	USA	712	≥65	EORTC QLQ-C30[a]	Mean (95 % CI[a]). RCT[a]: 12 months 82.1 (79.2–85.1), 24 months 80.2 (77.1–83.4). Observational study: 12 months 81.6 (79.3–83.8), 24 months 80.7 (78.2–83.1).
Marinac et al. (2014) [81]	USA	3,088	18–70	SF-36[a]	Younger participants had a significantly better physical functioning. Age (years), mean (SD[a]): lowest physical functioning tertile: 54.5 (9.0), second tertile: 52.8 (8.9), best physical functioning tertile: 50.5 (8.6) (p =<00.001).
Matalqah et al. (2011) [82]	Malaysia	150	23–83	EQ-5D-3L[a]	Decreased mobility: participants aged <50 years; participants with breast cancer diagnoses 11.5 %, control group of participants without breast cancer diagnoses 8.2 % (p-value: 0.543). Aged ≥50 years; participants with breast cancer diagnoses 37.0 %, control group 27.0 % (p-value = 1.000). Difficulty in self-care: participants aged <50 years; participants with breast cancer diagnoses 6.6 %, control group 1.6 % (p-value = 0.171). Aged ≥50 years; participants with breast cancer diagnoses 18.0 %, control group 9.0 % (p-value = 0.079). There were no significant differences between problems with mobility or self-care between participants with breast cancer diagnoses in both age groups when compared to the control group of participants without breast cancer diagnoses (p > 0.05 for both).
Maurer et al. (2021) [83]	Germany	1,123. 481 completed PROMs at just one follow-up.	≥54	EORTC QLQ-C30[a]	At around 5 years post-diagnosis, participants aged ≤64 years had a better physical functioning than participants aged ≥65. At around 10 years post-diagnosis, the participants aged ≤58 years had even better scores on their physical functioning, and participants aged ≥65 had declined. Physical functioning mean amongst participants aged ≤58 years: Around 5 years post-diagnosis 79.28, around 10 years post-diagnosis 83.10; control group 85.54. 59–64 years: Around 5 years post-diagnosis 81.49, around 10 years post-diagnosis 79.27; control group 80.12. ≥ 65 years: Around 5 years post-diagnosis 75.19, around 10 years post-diagnosis 71.59; control group: 70.65. Within each age group, participants after treatment for breast cancer were not significantly different to a control group of participants who did not have cancer diagnoses.
Michael et al. (2020) [84]	USA	1,636	50–79	SF-36[a]	The largest declines in physical functioning amongst participants who had breast cancer diagnoses when compared to participants who did not have breast cancer were amongst those aged ≥70 years. Participants aged 70–79 with regional breast cancer did not have significant physical functioning declines when compared to participants of this age group with localised breast cancer. However, for women aged < 59 years and aged 60–69 years, a higher stage of breast cancer (localised/regional) was associated with greater declines in physical

(*continued on next page*)

Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
					functioning. Participants with breast cancer diagnoses compared with participants without breast cancer diagnoses, difference-in-differences estimate (95 % CI[a]). Participants aged <50–59 years: localised breast cancer diagnoses −1.49 (−3.36 - 0.39), regional breast cancer diagnoses −4.50 (−7.60 to −1.40). Participants aged 60–69 years: localised 1.01 (−2.76 - 0.74), regional −7.22 (−10.7 to −3.78). Participants aged ≥70 years: localised 4.81(-7.91 to −1.71), regional −0.15 (−6.80 - 6.50).
Mosewich et al. (2013) [85]	Canada	358	≥18	SF-36[a]	Participants aged ≥60 years had a significantly poorer physical functioning than participants aged <60 years (t (355.24) = 2.29, p = 00.02).
Paskett et al. (2008) [86]	USA	5,021	50–79	SF-36[a]	Participants diagnosed with breast cancer aged >55 years had more difficulties with physical functioning (β = −1.62; p < 0.001) when compared to participants who had not had cancer.
Pires de Carvalho et al. (2019) [87]	Brazil	89	58–70	The Health Assessment Questionnaire	Age had no significant correlation with physical functioning.
Quinten et al. (2018) [88]	Belgium	109	70–90	EORTC QLQ-C30[a]	Older age was significantly associated with a poorer physical functioning in a correlation (p = 0.001). Physical functioning was significantly associated with nine aging parameters assessed in a correlation. From a graph mean physical functioning around 1 year and 1 month after surgery score for participants who received adjuvant chemotherapy about 75, those who did not receive chemotherapy about 60. No significant impact of chemotherapy on physical functioning.
Sehl et al. (2013) [89]	USA	Baseline = 689, 15 months = 491, 27 months = 451	≥65	SF-36[a]	Baseline mean score = 79, SD[a] = 25 (higher than reference values for the general population). Declines between baseline and 27 months.
Sleight et al. (2019) [90]	USA	102	35–78	SF-36[a]	Correlation between age and physical functioning: 0.25 (p < 0.05)
Wadasadawala et al. (2009) [91]	India	48	45–62	EORTC QLQ-C30[a]	Physical functioning, mean, median, SD[a]. APBI[a] - 85.8, 86.7, 12.30. WBRT[a] - 84.8, 86.7, 15.81. (p-value = 0.916).
Williams et al. (2011) [92]	UK	255	≥65	EORTC QLQ-C30[a]	There was a significant change over time (p < 0.0001, adjusted p < 0.0001). Mean difference: 0.45, 95 % CI[a]: 5.63-4.74. Physical functioning 15 months: 0.61, 5 years: 0.76 (p < 0.0001). This data represents physical functioning declining over time. Data on a graph shows physical functioning baseline levels at about 82 and for radiotherapy, 9 months after surgery around 79, 15 months around 77.5, 3 years the same, and 5 years around 73. For no radiotherapy 9 months after surgery around 77, 15 months 76, 3 years 77.5, and 5 years 74.
Winters-Stone et al. (2019) [13]	USA	84	≥60	SF-36[a]	Physical functioning significantly lower for breast cancer survivors than the control group. Mean (SD[a]): breast cancer survivors: 47.3 (9.1); control group: 52.9 (4.0), p < 0.001).
Xie et al. (2022) [93]	China	80	31–65	EORTC QLQ-C30[a]	After MRM[a] physical functioning score from graph about 75, after MRM[a] with neo-adjuvant chemotherapy about 88.
Young et al. (2014) [94]	USA	2,264	18–70	Ability to perform daily activities in the past month. Based on Framingham Disability Study, Established Populations	Participants who had difficulties with physical functioning were older. Age at diagnosis, number (%). All p < 0.0001:

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Table 1 (*continued*)

Reference (Authors, year)	Country	Number of participants with breast cancer	Age of participants (years)	PROMs used	Key physical functioning findings of studies with age sub-groups. (not all studies reported p-values)
				for Epidemiologic Studies of the Elderly, and Nagi, Rosow, and Breslau's measures.	<50 years: no limitations - 104 (36.6 %), with a limitation 317 (20.4 %) 50–64 years: no limitations - 131 (46.1 %), with a limitation 725 (46.6 %) 65–79 years: no limitations - 49 (17.3 %), with a limitation 515 (33.1 %)

[a] Abbreviations: SD = standard deviation, SE = standard error, CI = confidence interval, ADL = activities of daily living, CMF = cyclophosphamide, methotrexate, and fluorouracil [75], AC = doxorubicin and cyclophosphamide [75], ALND = axillary node dissection [55], SLNB = sentinel node surgery [55], MRM = modified radical mastectomy [66,93], BCS = breast-conserving surgery [66], APBI = accelerated partial breast irradiation [91], WBRT = whole breast radiotherapy [91], RCT = randomised clinical trial [80], EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer (EORTC) - Quality of Life of Cancer Patients [95] PF scores 0–100 (0 worse level of functioning, 100 higher level of functioning), EQ-5D-5L = EuroQol EQ-5D-5L [96] scoring of 5 dimensions with 5 levels: no problem, slight problem, moderate problem, severe problem, extreme problem. EQ-5D-3L = EuroQol EQ-5D-3L scoring of 5 dimensions with 3 levels: no problem, some problem, extreme problem. [97], SF-12 = Short Form 12, scoring of 8 domains 0–100 (0 worse physical and mental health, 100 higher physical and mental health). [98], SF-36 = Short Form 36 [99,100] scoring of 8 domains 0–100 (0 worse physical and mental health, 100 higher physical and mental health). Health Assessment Questionnaire [101], scoring of 8 sections, 0–3 (0 without any difficulty, 3 unable to do). Katz's ADL* Index [57] scoring of 6 functions 0–1 (1 dependence, 0 independent).

(Table 1).

3.2.2. Risk of bias (quality) assessment

A higher score indicated a study of higher quality and lower risk of bias (maximum score = 24, minimum score = zero) [51]. The range of scores was 17–24, with a mean of 20.3 (Appendix B). Six studies (13.6 %) had scores at the optimum end of the scale, with scores of 23–24 [56,58,71,73,74,84], and ten (22.7 %) were amongst the lower end of the range, with scores of 17–18 [53,72,59,60,67,76,77,79,91,93]. Studies scored poorly on aspects about confounding variables, the generalisability to the local population and follow-up period [51].

3.2.3. The overall impact of age on physical functioning

Twenty-nine (29 of 44, 65.9 %) of the studies that met the inclusion criteria and had age sub-groups had findings on the association between age and physical functioning. Nineteen of these studies (65.5 %) found that with older age, physical functioning declined post-breast cancer treatment [12,58,64,65,67,69,71,73,74,76,78,81,82,84,85,90,94,83,88]. These studies generally scored well on the risk of bias (quality) assessment, with a mean score of 21. Six studies (20.7 %) [72,62,70,77,79,87] found that age did not have a significant impact on physical functioning. These studies had a slightly lower mean score of 19 on the risk of bias (quality) assessment.

Three studies [58,63,94] reported on the percentage of physical functioning limitations by age groups: under 50 years, two studies reported a physical functioning limitation in 18 % [58] and 20 % [94]; for participants aged 50–64 years, two studies reported 43 % [58] and 47 % [94]; and for participants aged 65 years or over, three studies reported 33 % [94], 37 % [63] and 39 % [58].

Three studies reported on physical functioning amongst one particular age group. One study found that participants aged 65 years or over had physical functioning declines around two years post-diagnosis [89]. One other study found that participants aged 55 years or over who were post-menopausal had physical functioning declines immediately following chemotherapy or radiotherapy, but no further changes between this point in time and five years post-treatment [61]. Another study found that participants aged 69 years or over had physical functioning declines at six and 12 months post-diagnosis, but not six weeks, 18 months, or 24 months [56].

3.2.4. The impact of the stage of breast cancer on physical functioning

There were seven studies that included findings on the association between the stage of breast cancer and physical functioning. Three studies [57,81,88] found participants had less struggles with physical functioning if their cancer was of a lower stage. A fourth study [84] found that this was true for participants aged under 70 years, but not participants aged 70–79 years. Another study [67] found that the stage of breast cancer was significantly associated with physical functioning, although it did not state in what direction the association is. This study had a lower risk of bias (quality) assessment score. On the other hand, two studies [58,90] found that the stage of breast cancer was not associated with participants' physical functioning.

3.2.5. The impact of the type of treatment on physical functioning

Eight studies included participants who had undergone surgery as one of their forms of treatment. One study [76] found that participants had significant physical functioning declines post-surgery, although this study had one of the lower risk of bias (quality) assessment scores. Alternatively, three studies [66,67,70] found no significant difference in physical functioning when comparing a mastectomy and breast-conserving surgery. Participants in two studies [72,58] had a significantly better physical functioning after breast-conserving surgery than a mastectomy. Two studies [55,70] found that participants had no significant difference in their physical functioning after a sentinel lymph node biopsy or axillary lymph node dissection.

Nine studies had findings specifically on chemotherapy, although participants may have also completed other types of treatment, such as surgery and radiotherapy. In the initial weeks following chemotherapy, one study [77] found that participants had physical functioning declines after four weeks and one study [56] found that participants did not have physical functioning declines after six weeks. Amongst the studies exploring physical functioning between around six months and one year post-chemotherapy, one study [93] found that participants who had undergone neo-adjuvant chemotherapy had improvements in physical functioning, one study [56] found that participants had physical functioning declines, and one study [88] found that there was no impact on physical functioning. At an average of 15 months post-chemotherapy, one study [68] found that participants who had received chemotherapy did not have significant declines in physical functioning, and another study [56] found that this was also the case at 18 and 24 months. However, at an average of 21 months post-diagnosis, one study [94] found that participants who had received chemotherapy had declines in physical functioning. One study [58] found that a higher percentage of participants without physical functioning limitations received chemotherapy. Turning to the impact of the type of chemotherapy, one study [59] found that the type of chemotherapy received had an influence on physical functioning when finishing the treatment and four months thereafter. Another study [75] found that the type of chemotherapy only had an influence within the first month of finishing the treatment, but not at 12, 18, or 24 months afterwards.

Five studies reported results related to radiotherapy, although participants may have also completed other types of treatment, such as

surgery and chemotherapy. One study [58] found that a higher percentage of participants had physical functioning issues after receiving radiotherapy. However, in this study, a higher percentage of participants without physical functioning issues also received radiotherapy [58]. Two studies [55,77] found that participants had improvements in physical functioning six weeks post-radiotherapy. However, one study [92] found that participants had no significant difference in physical functioning after radiotherapy. One study [91] found that the type of radiotherapy received did not impact on physical functioning.

One study reported results on the type of hormone therapy received [78] and found that this did not have an impact on physical functioning.

3.2.6. The impact of the time after treatment on physical functioning

There were nine studies that included the influence of the time after treatment. Three studies [61,78,92] found that after five years, participants had deteriorations in physical functioning. However, one study [74] found that participants had improvements in physical functioning between five and ten years, and similarly between ten and 15 years post-diagnosis. These studies comprised a range of age groups [61,74,78,92]. Alternatively, one study [56] with participants aged 69 years or over found that although chemotherapy had a negative impact on physical functioning at six and 12 months post-diagnosis, it did not at six weeks, 18 months, or 24 months. One study [83] found that participants aged below 59 had improvements in their physical functioning between three and eight years after diagnosis, whereas participants aged 65 years or above had deteriorations in physical functioning within the same time frame. Alternatively, one study [90] that included participants with a wide range of ages found that physical functioning did not significantly correlate with the time post-diagnosis. Amongst studies measuring physical functioning within the first four months after treatment, one study [60] found that participants aged 55–77 years had physical functioning declines four months after receiving treatment. Another study [77] found that participants aged under 70 years had improvements in physical functioning between four weeks post-chemotherapy and six weeks post-radiotherapy.

3.2.7. The impact of comorbidities on physical functioning

Seven studies reported findings on the association between comorbidities and physical functioning, and all of these studies found that having a comorbidity was associated with declines in physical functioning. Five studies [12,58,64,67,90] had participants from a range of age groups, and two included only 'older' participants [13,89].

3.3. Secondary review questions

3.3.1. PROMs used

There were 28 different types of PROM used to measure physical functioning (Table 2). The most common was the EORTC QLQ-C30, used by half (50.6 %) the studies. The second most regularly used was the SF-36, by nearly one-third (32.3 %). The third most frequent option was to use a study-specific PROM (6.7 %).

3.3.2. Terms/labels used when referring to physical functioning

There were 145 different terms/labels used to refer to physical functioning. Those used by five or more studies are shown in Table 3. 'Physical functioning/function' was used most frequently (135/164 studies, 82.3 %).

The studies that used the EORTC QLQ-C30 or SF-36 (n = 132) follow a similar pattern, using 'physical functioning/function' in most cases (n = 126, 95.5 %), likely due to the recommended names of the corresponding scales. However, amongst the studies that use a PROM other than the EORTC QLQ-C30 or SF-36, 'physical functioning/function' is no longer most commonly used, being used by 28.1 % of studies (Table 3). The terms/labels used more frequently are 'mobility' (34.4 %), 'function/functions/functioning/functionality/functional' (31.3 %), 'walk/walking' (28.1 %) and 'daily activities/activity' (28.1 %) (Table 3).

Table 2
PROMs used to measure physical functioning.

PROM	Number (%) of studies (n = 164)
European Organization for Research and Treatment of Cancer (EORTC) - Quality of Life of Cancer Patients (EORTC QLQ-C30) [95]	83 (50.6 %)
Short Form 36 (SF-36) [99,100]	53 (32.3 %)
Study-specific	11 (6.7 %)
EuroQol EQ-5D-3L [97]	4 (2.4 %)
Nagi's physical performance scale [102]	1 (0.6 %) + 3 (1.8 %) more that were study-specific, based on Nagi
Short Form 12 (SF-12) [98]	4 (2.4 %)
Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) [103]	3 (1.8 %)
EuroQol EQ-5D-5L [96]	3 (1.8 %)
Based on Framingham Disability Study [104]	2 (1.2 %)
Based on Established Populations for Epidemiologic Studies of the Elderly [105]	2 (1.2 %)
Katz's Activities of Daily Living (ADL) Index [106]	2 (1.2 %)
EORTC Quality of Life of Breast Cancer Patients (EORTC QLQ-BR23)[a] [107]	1 (0.6 %)
EORTC Quality of Life Questionnaire - Chemotherapy-Induced Peripheral Neuropathy (EORTC QLQ-CIPN20) [108]	1 (0.6 %)
Functional Independence Measure [as cited by 109]	1 (0.6 %)
Health Assessment Questionnaire [101]	1 (0.6 %)
Holistic Needs Assessment [as cited by 110]	1 (0.6 %)
International Classification of Functioning, Disability and Health (ICF) checklist [111]	1 (0.6 %)
ICF Brief Core Set for breast cancer [as cited by 112]	1 (0.6 %)
ICF Comprehensive Core Set for breast cancer [as cited by 113]	1 (0.6 %)
International Physical Activity Questionnaire (IPAQ) [114]	1 (0.6 %)
Kwan's arm problem scale [115]	1 (0.6 %)
Long-term quality of life breast cancer scale (LTQOL-BC) [116]	1 (0.6 %)
Patient Care Monitor [117]	1 (0.6 %)
Perceived Impact of Problem Profile [118]	1 (0.6 %)
Pulmonary Functional Status and Dyspnea Questionnaire [as cited by 119]	1 (0.6 %)
Quick DASH [120]	1 (0.6 %)
Shoulder Rating Questionnaire [121]	1 (0.6 %)
World Health Organization Quality of Life questionnaire (WHOQOL-BREF) [122]	1 (0.6 %)

[a] It is recognised that the EORTC QLQ-BR23 is not intended for measuring physical functioning. However, the study using it [123] only included three EORTC QLQ-BR23 questions, one asking whether participants can lift or move their arm and reported on the questions separately.

'Mobility' tended to be used most frequently by studies using the EuroQol EQ-5D-3L or EQ-5D-5L (Appendix C). However, 'function/functions/functioning/functionality/functional', 'walk/walking' and 'daily activities/activity' were most consistently used across the study-specific PROMs, including those that were based on the Framingham Disability Study or Established Populations for Epidemiologic Studies of the Elderly, and Nagi's physical performance scale (Appendix C). The terms/labels referring to specific aspects of physical functioning such as 'carry/carrying' and 'reach/reaching', tended to be used by the studies using study-specific PROMs including those based on the Framingham Disability Study or Established Populations for Epidemiologic Studies of the Elderly, Nagi's physical performance scale, or the DASH (Appendix C).

4. Discussion

This systematic review explored whether physical functioning measured by PROMs after treatment for early-stage localised breast cancer was associated with age, as well as the PROMs used and

Table 3
The terms/labels that were used by five or more studies, shown by the number and percentage of all the studies, and those using the EORTC QLQ-C30, SF-36, or a different PROM.

Term/label	All studies (n = 164)	EORTC QLQ-C30 (n = 83)	SF-36 (n = 53)	Not using EORTC QLQ-C30 or SF-36 (n = 32)
physical functioning/ function	135 (82.3 %)	81 (97.6 %)	49 (92.5 %)	9 (28.1 %)
function/functions/ functioning/ functionality/ functional	18 (11.0 %)	6 (7.2 %)	3 (5.7 %)	10 (31.3 %)
mobility	18 (11.0 %)	3 (3.6 %)	4 (7.5 %)	11 (34.4 %)
walk/walking	18 (11.0 %)	6 (7.2 %)	3 (5.7 %)	9 (28.1 %)
self-care	15 (9.1 %)	4 (4.8 %)	4 (7.5 %)	7 (21.9 %)
daily activities/activity	14 (8.5 %)	3 (3.6 %)	2 (3.8 %)	9 (28.1 %)
dressing/getting dressed/whether can dress	14 (8.5 %)	3 (3.6 %)	3 (5.7 %)	8 (25.0 %)
functional limitation/ limitations	14 (8.5 %)	3 (3.6 %)	6 (11.3 %)	6 (18.8 %)
lift/lifting	12 (7.3 %)	1 (1.2 %)	3 (5.7 %)	8 (25.0 %)
activities of daily living	11 (6.7 %)	4 (4.8 %)	2 (3.8 %)	5 (15.6 %)
carry/carrying	11 (6.7 %)	2 (2.4 %)	2 (3.8 %)	7 (21.9 %)
functional status	10 (6.1 %)	3 (3.6 %)	4 (7.5 %)	3 (9.4 %)
walking up and down/ climbing/climb stairs/ walking stairs	9 (5.5 %)	2 (2.4 %)	3 (5.7 %)	4 (12.5 %)
activity/activities	8 (4.9 %)	4 (4.8 %)	2 (3.8 %)	3 (9.4 %)
functional impairment/ impairments	8 (4.9 %)	1 (1.2 %)	1 (1.9 %)	6 (18.8 %)
movement/movements/ move	8 (4.9 %)	0 (0.0 %)	5 (9.4 %)	3 (9.4 %)
physical activity/ activities	8 (4.9 %)	4 (4.8 %)	3 (5.7 %)	1 (3.1 %)
reach/reaching	8 (4.9 %)	0 (0.0 %)	1 (1.9 %)	7 (21.9 %)
wash/washing	8 (4.9 %)	3 (3.6 %)	0 (0.0 %)	5 (15.6 %)
bathing	7 (4.3 %)	2 (2.4 %)	2 (3.8 %)	3 (9.4 %)
eating	7 (4.3 %)	3 (3.6 %)	0 (0.0 %)	4 (12.5 %)
functional capacity	7 (4.3 %)	1 (1.2 %)	3 (5.7 %)	3 (9.4 %)
range of motion	7 (4.3 %)	0 (0.0 %)	0 (0.0 %)	7 (21.9 %)
physical limitation/s	6 (3.7 %)	2 (2.4 %)	3 (5.7 %)	1 (3.1 %)
strength	6 (3.7 %)	0 (0.0 %)	2 (3.8 %)	4 (12.5 %)
arm/upper extremity/ shoulder/upper limb mobility/mobility of joint function/s	5 (3.0 %)	1 (1.2 %)	1 (1.9 %)	3 (9.4 %)
functional decline/s	5 (3.0 %)	1 (1.2 %)	2 (3.8 %)	2 (6.3 %)
kneeling	5 (3.0 %)	0 (0.0 %)	1 (1.9 %)	4 (12.5 %)
physical health	5 (3.0 %)	1 (1.2 %)	2 (3.8 %)	2 (6.3 %)
pushing/push	5 (3.0 %)	0 (0.0 %)	0 (0.0 %)	5 (15.6 %)
sitting	5 (3.0 %)	1 (1.2 %)	0 (0.0 %)	4 (12.5 %)
standing	5 (3.0 %)	1 (1.2 %)	0 (0.0 %)	4 (12.5 %)
stay in/confined to/get/ getting in and out of bed/chair	5 (3.0 %)	3 (3.6 %)	1 (1.9 %)	1 (3.1 %)

variations in language when referring to physical functioning. The complexity of the physical functioning concept was highlighted, with studies using 28 different types of PROM, 145 terms/labels for physical functioning, and researching physical functioning from a variety of different angles: focusing on different sub-groups, and breaking sub-groups down in different ways i.e. varying cut-off points for 'younger' and 'older' age groups, times post-treatment and specifying different treatment types and in different levels of specificity. This variability was reflected in the fact that only 29 of the 44 studies with age sub-groups included findings on the association between age and physical functioning. Of these, most (65.5 %) tended to point towards participants of an older age having more physical functioning declines post-treatment than younger participants. However, one-fifth (20.7 %) found that age was not associated with physical functioning limitations, and the remaining studies did not report findings in a format enabling physical functioning findings to be summarised by age groups.

Systematic reviews within the field of physical functioning after treatment for cancer include Hidding et al. (2014), who included physical functioning aspects but only involving the upper musculoskeletal system and forms of assessment were not limited to PROMs [10]. Atkinson et al. (2017) explored the psychometric properties of PROMs but did not focus on breast cancer patients [21]. Harrington et al. (2020) conducted a systematic scoping review rather than a systematic review exploring physical functioning PROMs used in oncology and included participants other than just those with breast cancer, as well as metastatic cancers, and measures other than exclusively PROMs that were also used before and during treatment, or in palliative care [20].

The finding of this systematic review that most studies pointed towards increasing age being associated with physical functioning declines post-treatment, is based on studies that were mostly of a high quality and low risk of bias and is in line with the previously published national data from NHS England [15].

However, it is difficult to determine whether this decline is due solely to the effects of treatment or if an element of this decline is due to aging and the increasing comorbidities that older people face, which could affect their physical functioning [124]. Comparisons with general population data would be helpful in those studies [125]. Moreover, when using PROs to measure physical functioning one is relying on the respondents' assessment of their physical functioning rather than their actual performance. In future studies, wearable devices that are increasingly available may be added for accurate assessment of physical functioning in patients after cancer treatments [126,127].

The most common standard questionnaires used in this systematic review have a small number of items on physical functioning (5 in EORTC QLQ-C30 and 10 in SF36). Typically, they do not capture well higher levels of functioning (i.e. have a ceiling effect), may not detect smaller changes in physical functioning over time, or smaller differences between younger versus older patients. Modern measurement methods such as Computer Adaptive Testing have the potential to overcome these issues and could be recommended for future use [128, 129[133, 134]. When using the EORTC QLQ-C30 with clinical anchors to help interpret scores and determine minimal importance differences (MID) it is capable of successfully detecting meaningful change [130,131]. However, these methodological studies focused on advanced breast cancer

only and the data on early breast cancer is limited.

This systematic review is also in concordance with previous reviews in finding that the EORTC QLQ-C30 and SF-36 were most frequently used to measure physical functioning [21,20]. This is understandable as these PROMs were of key importance when the physical functioning concept was first developed, are widely known, and have been considered reliable and valid PROMs for many years [95,99,100]. Atkinson et al.'s (2017) [21] and Harrington et al.'s (2020) [20] reviews found that the SF-36 was used in a similar percentage of studies as this systematic review (32.3 %). However, the percentage of studies (50.6 %) that used the EORTC QLQ-C30 was around the mid-point of the findings from Atkinson et al.'s (2017) (67 %) and Harrington et al.'s (2020) (21.5 %) reviews [21,20].

There were huge variations in the term/label used to refer to physical functioning [20,18]. However, 'physical functioning/function' was used by most studies. This was possibly due to these terms/labels being used as the names of the scales in the EORTC QLQ-C30 and SF-36 [95,99,100,132]. Amongst the studies using PROMs other than the EORTC QLQ-C30 and SF-36, 'physical functioning/function' was used less frequently than 'mobility' and 'function/functions/functioning/functionality/functional', and as frequently as 'walk/walking' and 'daily activities/activity' (Table 3). Amongst these studies using other PROMs, there was increased reference to specific aspects of physical functioning, the most common being 'mobility', 'walking', 'self-care', 'getting dressed', 'lifting', 'carrying', 'reaching' and 'range of motion' (Table 3). This may be explained as authors may be more likely to specify the individual aspects stated in these PROMs with the PROMs being less widely used. The EORTC QLQ-C30 and SF-36 encompass these aspects but do not specifically state the terms/labels 'mobility', 'self-care', 'reaching', or 'range of motion' and the EORTC QLQ-C30 does not specifically state 'lifting' [95,100]. These aspects are encompassed by Stewart and Kamberg's (1992) definition of physical functioning, and it may be beneficial for these more specific terms/labels to be used more widely within the field [47].

This systematic review used broad search terms (Appendix A) due to the possibility of studies meeting the inclusion criteria that did not specifically aim to measure physical functioning, but instead aiming to measure other concepts such as quality of life, in which physical functioning was one of the measured components. Of the 44 studies with age sub-groups, only seven (15.9 %) specifically aimed to measure physical functioning post-treatment [12,13,57,68,84,87,94]. This reflects the need for increased awareness, further development of knowledge and research with a specific focus on physical functioning after treatment for breast cancer [9,10].

All studies reporting on comorbidities consistently found that having a comorbidity was associated with declines in physical functioning. However, findings from other sub-groups (stage of breast cancer, type of treatment and time after treatment) are too varied, and those that have concordance are too few to make any conclusions. This may be due to the large number of factors, that aside from age, may influence physical functioning. Many factors can interplay when measuring physical functioning, making it difficult to isolate any one factor, and resulting in studies researching many different aspects of the complex concept. However, there are some instances in which there is a trend towards some consistency within the findings. The evidence points towards participants of a lower stage of early-stage breast cancer having less struggles with physical functioning, or their physical functioning not being affected. This may be explained due to higher stages and the associated treatment having more pronounced late effects. It was not possible to determine the possible trajectory of physical functioning over time post-treatment due to the variations in time intervals of physical functioning assessments between studies. However, findings point towards participants having declines in physical functioning five years post-treatment. This is in concordance with most studies finding that an older age was associated with physical functioning declines post-treatment. However, with a longer follow-up post-treatment, it may become more difficult to distinguish between aging and the ongoing impact of the time post-treatment. Participants may have a response shift and become used to a new level of physical functioning with increasing time post-treatment [133]. Therefore, participants may rate their physical functioning less favourably [133].

Studies on surgery focused on investigating the influence of different types of breast cancer surgery, rather than surgery in general. They were comparing specific sub-groups of types of surgery i.e. mastectomy vs. breast-conserving surgery, or were comparing sentinel lymph node biopsy vs axillary lymph node dissection rather than presenting results on undergoing surgery for breast cancer in general. Therefore, an overall finding in terms of physical functioning post-surgery was not possible to determine [44–46,134,5]. The chemotherapy findings have a lack of consensus, with studies having contrasting findings even when broken down by those with similar time intervals post-treatment. When considering the radiotherapy findings, Levangie and Drouin's (2009), and Hidding et al.'s (2014) systematic reviews concluded that radiotherapy had negative impacts on physical functioning [135,10]. The radiotherapy findings in this systematic review are less consistent. However, they are only based on five studies, three in which participants had only recently finished radiotherapy. Considering the large-scale trials that have been conducted on hormone therapy, it is surprising that only one study [78] had findings on physical functioning after hormone therapy. However, a few studies on hormone therapy did not meet the inclusion criteria for the aspect of the systematic review with age sub-groups. In addition, amongst the other studies with age sub-groups, participants may have been receiving hormone therapy, but the studies did not look at the effect of hormone therapy specifically on physical functioning.

4.1. Limitations

The large volume of literature on breast cancer and PROMs amplified the possibility of the literature screening, data extraction and risk of bias (quality) assessment being impacted by subjective interpretation, or manual errors and more prone to omissions. However, two other researchers conducted checks and/or discussed any discrepancies with the primary researcher. The systematic review only included literature in English. Therefore, it is possible that relevant studies in other languages could have been missed.

It was not possible to use meta-analysis due to the heterogeneity in the data. Therefore, the method of data synthesis may be less robust [52]. However, using Cambell's (2020) guidance, the data was grouped by similar themes, and arranged by PROMs and risk of bias (quality) assessment scores in tables before being synthesised through narrative [52]. Therefore, a formal method of data synthesis was followed as far as possible.

4.2. Conclusions

This systematic review highlighted the complexity of researching the physical functioning concept after breast cancer treatment. Studies with consistent methods of reporting the association between age and physical functioning tended to point towards participants of an older age having more physical functioning declines. However, it is not possible to determine if this decline is only due to treatment or if effects of aging also play a role. In addition, EORTC QLQ-C30 physical functioning items alone could fail to detect changes within patients with higher functioning levels if not used with MIDs. Computer Adaptive Testing has the potential to overcome these issues and could be recommended for future use. Comorbidities were found to be associated with physical functioning declines, but it was not possible to determine other sub-groups at increased risk. A variety of PROMs were used and a wealth of terms/labels for physical functioning. The PROM used most frequently was the EORTC QLQ-C30, followed by the SF-36, and the term/label used most often was 'physical functioning/function'. However, physical

functioning was often measured as a component within studies focusing on a broader concept, so the PROMs and language identified may lack specificity. This reflects the need for increased awareness, focused research and further development of knowledge within the topic area [9, 10]. To aid universal understanding, it may be beneficial to health professionals if 'gold standards' of physical functioning PROMs and terms/labels are established.

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Ethical approval

Ethical approval was not required.

CRediT authorship contribution statement

V.R. Robins: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **S. Gelcich:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **K. Absolom:** Writing – review & editing, Supervision, Conceptualization. **G. Velikova:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

Professor Galina Velikova has the following conflicts of interest:
Honoraria:
Pfizer, Novartis, Eisai.
Advisory boards:
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2024.103734.

References

[1] Yeo W, Pang E, Liem GS, Suen JJS, Ng RYW, Yip CCH, Li L, Yip CW, et al. Menopausal symptoms in relationship to breast cancer-specific quality of life after adjuvant cytotoxic treatment in young breast cancer survivors. Health Qual Life Outcome 2020;18(1):24. https://doi.org/10.1186/s12955-020-1283-x.
[2] Schreier AM, Johnson LA, Vohra NA, Muzaffar M, Kyle B. Post-treatment symptoms of Pain, Anxiety, Sleep Disturbance, and Fatigue in breast cancer survivors. Pain Manag Nurs 2019;20(2):146–51. https://doi.org/10.1016/j.pmn.2018.09.005.
[3] Jefford M, Rowland J, Grunfeld E, Richards M, Maher J, Glaser A. Implementing improved post-treatment care for cancer survivors in England, with reflections from Australia, Canada and the USA. Br J Cancer 2013;108(1):14–20. https://doi.org/10.1038/bjc.2012.554.
[4] Maddams J, Utley M, Moller H. Projections of cancer prevalence in the United Kingdom, 2010-2040. Br J Cancer 2012;107(7):1195–202. https://doi.org/10.1038/bjc.2012.366.
[5] Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, Zackrisson S, Senkus E, on behalf of the ESMO Guidelines Committee. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2019;30(8):1194–220. https://doi.org/10.1093/annonc/mdz173.
[6] Office for National Statistics (ONS). Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed. [Accessed 8 March 2021].
[7] Moschetti I, Cinquini M, Lambertini M, Levaggi A, Liberati A. Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev 2016;(5):CD001768. https://doi.org/10.1002/14651858.CD001768.pub3.
[8] Kirshbaum MN, Dent J, Stephenson J, Topping AE, Allinson V, McCoy M, Brayford S. Open access follow-up care for early breast cancer: a randomised controlled quality of life analysis. Eur J Cancer Care 2017;26(4). https://doi.org/10.1111/ecc.12577.
[9] Fontein DB, de Glas NA, Duijm M, Bastiaannet E, Portielje JE, Van de Velde CJ, Liefers GJ. Age and the effect of physical activity on breast cancer survival: a systematic review. Cancer Treat Rev 2013;39(8):958–65. https://doi.org/10.1016/j.ctrv.2013.03.008.
[10] Hidding JT, Beurskens CH, van der Wees PJ, van Laarhoven HW, Nijhuis-van der Sanden MW. Treatment related impairments in arm and shoulder in patients with breast cancer: a systematic review. PLoS One 2014;9(5):e96748. https://doi.org/10.1371/journal.pone.0096748.
[11] World Health Organization (WHO). World report on ageing and health. Available from: https://www.who.int/publications/i/item/9789241565042. [Accessed 23 February 2021].
[12] Cohen HJ, Lan L, Archer L, Kornblith AB. Impact of age, comorbidity and symptoms on physical function in long-term breast cancer survivors (CALGB 70803). J Geriatr Oncol 2012;3(2):82–9.
[13] Winters-Stone KM, Medysky ME, Savin MA. Patient-reported and objectively measured physical function in older breast cancer survivors and cancer-free controls. Journal of Geriatric Oncology 2019;10(2):311–6.
[14] Avis NE, Deimling GT. Cancer survivorship and aging. Cancer. 2008;113(12 Suppl):3519–29. https://doi.org/10.1002/cncr.23941.
[15] NHS. Cancer quality of life survey (v.3.3.1 (3c)). National disease registration service. 2023. Available from: https://www.cancerdata.nhs.uk/cancerqol. [Accessed 12 October 2023].
[16] Derks MG, de Glas NA, Bastiaannet E, de Craen AJ, Portielje JE, van de Velde CJ, van Leeuwen FE, Lifers GJ. Physical functioning in older patients with breast cancer: a prospective cohort study in the TEAM trial. Oncol 2016;21(8):946–53. https://doi.org/10.1634/theoncologist.2016-0033.
[17] Petersen MA, Groenvold M, Aaronson NK, Chie WC, Conroy T, Costantini A, Fayers P, Helbostad J, et al., on behalf of the EORTC Quality of Life Group. Development of computerised adaptive testing (CAT) for the EORTC QLQ-C30 dimensions - general approach and initial results for physical functioning. Eur J Cancer 2010;46(8):1352–8. https://doi.org/10.1016/j.ejca.2010.02.011.
[18] Bennett JA, Winters-Stone K, Nail L. Conceptualizing and measuring physical functioning in cancer survivorship studies. Oncol Nurs Forum 2006;33(1):41–9.
[19] Freiberger E, de Vreede P, Schoene D, Rydwik E, Mueller V, Frandin K, Hopman-Rock M. Performance-based physical function in older community-dwelling persons: a systematic review of instruments. Age Ageing 2012;41(6):712–21. https://doi.org/10.1093/ageing/afs099.
[20] Harrington SE, Stout NL, Hile E, Fisher MI, Eden M, Marchese V, Pfalzer LA. Cancer rehabilitation publications (2008–2018) with a focus on physical function: a scoping review. Phys Ther 2020;100(3):363–415.
[21] Atkinson TM, Stover AM, Storfer DF, Saracino RM, D'Agostino TA, Pergolizzi D, Matsoukas K, Li Y, et al. Patient-reported physical function measures in cancer clinical trials. Epidemiol Rev 2017;39(1):59–70. https://doi.org/10.1093/epirev/mxx008.
[22] Kirkhus L, Harneshaug M, Benth JŠ, Grønberg BH, Rostoft S, Bergh S, Hjermstad MJ, Slbæk G, et al. Modifiable factors affecting older patients' quality of life and physical function during cancer treatment. J Geriatr Oncol 2019;10(6):904–12. https://doi.org/10.1016/j.jgo.2019.08.001.
[23] Painter P, Stewart AL, Carey S. Physical functioning: definitions, measurement, and expectations. Adv Ren Replace Ther 1999;6(2):110–23.
[24] Life Options Rehabilitation Program. Physical functioning assessment: a tool for improving quality of life on dialysis. Renal Rehabilitation Report 1999;7(6):4–5 [Amgen Inc].
[25] Edemekong PF, Bomgaars DL, Sukumaran S, Levy SB. Activities of daily living. StatPearls 2020 [Treasure Island: Florida].
[26] Hopkins RO, Suchyta MR, Kamdar BB, Darowski E, Jackson JC, Needham DM. Instrumental activities of daily living after critical illness: a systematic review. Ann Am Thorac Soc 2017;14(8):1332–43. https://doi.org/10.1513/AnnalsATS.201701-059SR.
[27] Buffart LM, Kalter J, Sweegers MG, Courneya KS, Newton RU, Aaronson NK, Jacobsen PB, May AM, et al. Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs. Cancer Treat Rev 2017;52:91–104. https://doi.org/10.1016/j.ctrv.2016.11.010.

[28] Brown JC, Harhay MO, Harhay MN. Physical function as a prognostic biomarker among cancer survivors. Br J Cancer 2015;112(1):194–8. https://doi.org/10.1038/bjc.2014.568.

[29] Brown JC, Harhay MO, Harhay MN. Patient-reported versus objectively-measured physical function and mortality risk among cancer survivors. J Geriatr Oncol 2016;7(2):108–15. https://doi.org/10.1016/j.jgo.2016.01.009.

[30] Rossi A, Colantuoni G, Maione P, Ferrara C, Airoma G, Barzelloni ML, Castaldo V, Gridelli C. Chemotherapy of breast cancer in the elderly. Curr Med Chem 2005;12(3):297–310. https://doi.org/10.2174/0929867053363261.

[31] Muss HB, Berry DA, Cirincione CT, Theodoulou M, Mauer AM, Kornblith AB, Partridge AH, Dressler LG, et al. Adjuvant chemotherapy in older women with early-stage breast cancer. CALGB. N Engl J Med 2009;360:2055–65. https://doi.org/10.1056/NEJMoa0810266.

[32] Biganzoli L, Wildiers H, Oakman C, Marotti L, Loibl S, Kunkler I, Reed M, Ciatto S, et al. Management of elderly patients with breast cancer: updated recommendations of the international society of geriatric oncology (SIOG) and European society of breast cancer specialists (EUSOMA). Lancet Oncol 2012;13(4):e148–60.

[33] Leonard RC, Barrett-Lee PJ, Gosney MA, Willett AM, Reed MW, Hammond PJ. Effect of patient age on management decisions in breast cancer: consensus from a national consultation. Oncol 2010;15:657–64.

[34] Bottomley, A., Reijneveld, J. C., Koller, M., Flechtner, H., Tomaszewski, K. A. and Greimel, E., On behalf of the 5th EORTC Quality of Life in Cancer Clinical Trials Conference Faculty. 2019. Current state of quality of life and patient-reported outcomes research. Eur J Cancer. 121, pp.55-63. doi:10.1016/j.ejca.2019.08.016.

[35] Black N. Patient reported outcome measures could help transform healthcare. BMJ 2013;346:f167. https://doi.org/10.1136/bmj.f167.

[36] Basch E, Charlot M, Dueck AC. Population-level evidence of survival benefits of patient-reported outcome symptom monitoring software systems in routine cancer care. Cancer Med 2020;9(21):7797–9. https://doi.org/10.1002/cam4.3480.

[37] Kotronoulas G, Kearney N, Maguire R, Harrow A, Di Domenico D, Croy S, MacGillivray S. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 2014;32(14):1480–501. https://doi.org/10.1200/JCO.2013.53.5948.

[38] Nama V, Nordin A, Bryant A. Patient-reported outcome measures for follow-up after gynaecological cancer treatment. Cochrane Database Syst Rev 2013;(11):CD010299. https://doi.org/10.1002/14651858.CD010299.pub2.

[39] van Egdom LSE, Oemrawsingh A, Verweij LM, Lingsma HF, Koppert LB, Verhoef C, Klazinga N, Hazelzet JA. Implementing patient-reported outcome measures in clinical breast cancer care: a systematic review. Value Health 2019;22(10):1197–226. https://doi.org/10.1016/j.jval.2019.04.1927.

[40] Berry DL. Patient-reported symptoms and quality of life integrated into clinical cancer care. Semin Oncol Nurs 2011;27(3):203–10. https://doi.org/10.1016/j.soncn.2011.04.005.

[41] U.S. Department of Health and Human Services. Food and Drug Administration. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. Clinical/Medical; 2009. Available from: https://www.fda.gov/media/77832/download. [Accessed 24 October 2023].

[42] Robins V, Gelcich S, Velikova G, Absolom K. The impact of age on physical functioning after treatment for breast cancer, as measured by patient-reported outcome measures: a systematic review. PROSPERO 2021. CRD42021235320. [Online]. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021235320; 2021.

[43] Cancer Research UK. About breast cancer staging and grades. Available from: https://www.cancerresearchuk.org/about-cancer/breast-cancer/stages-types-grades/about-breast-cancer-staging-grades. [Accessed 9 February 2021].

[44] NHS. Overview: breast cancer in women. Available from: https://www.nhs.uk/conditions/breast-cancer/. [Accessed 9 February 2021].

[45] NHS. Treatment: breast cancer in women. Available from: https://www.nhs.uk/conditions/breast-cancer/treatment/. [Accessed 9 February 2021].

[46] Cancer Research UK. Treatment options. Available from:. 2020. https://www.cancerresearchuk.org/about-cancer/breast-cancer/treatment/treatment-decisions. [Accessed 9 February 2021].

[47] Stewart AL, Kamberg CJ. Chapter 6: physical functioning measures. In: Stewart AL, Ware JE, editors. Measuring functioning and well-being: the medical outcomes study approach. Durham and London: Duke University Press; 1992. p. 86.

[48] Amireault S, Godin G. The Godin-Shephard Leisure-Time Physical Activity Questionnaire: validity evidence supporting its use for classifying healthy adults into active and insufficiently active categories. Percept Mot Skills: Physical Development and Measurement 2015;120(2):604–22.

[49] FACIT.org. FACIT measures & languages. Available from: https://www.facit.org/measures-language-availability. [Accessed 14 November 2023].

[50] Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6(7):e1000097. https://doi.org/10.1371/journal.pmed1000097.

[51] Critical Appraisal Skills Programme. CASP (cohort study) checklist. Available from: https://casp-uk.net/casp-tools-checklists/; 2018.

[52] Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, Hartmann-Boyce J, Ryan R, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. BMJ 2020;368. https://doi.org/10.1136/bmj.l6890.

[53] Arraras JI, Manterola A, Dominguez MA, Arias F, Villafranca E, Romero P, Martinez E, Illarramendi JJ, Salgado E. Impact of radiotherapy on the quality of life of elderly patients with localized breast cancer. A prospective study. Clin Transl Oncol: Official Publication of the Federation of Spanish Oncology Societies & of the National Cancer Institute of Mexico 2008;10:498–504.

[54] Arraras JI, Illarramendi JJ, De La Cruz S, Asin G, Manterola A, Ibanez B, Salgado E, Cambra K, et al. Quality of life in long-term premenopausal early-stage breast cancer survivors from Spain. Effects of surgery and time since surgery. Journal of B.U.ON. 2016;21:1090–8.

[55] Arraras JI, Manterola A, Asin G, Illarramendi JJ, Cruz SDL, Ibanez B, Delfrade J, Salgado E, et al. Quality of life in elderly patients with localized breast cancer treated with radiotherapy. A prospective study. Breast 2016;26:46–53.

[56] Battisti NML, Reed MWR, Herbert E, Morgan JL, Collins KA, Ward SE, Holmes GR, Bradburn M, et al. Bridging the Age Gap in breast cancer: impact of chemotherapy on quality of life in older women with early breast cancer. Eur J Cancer 2021;144:269–80.

[57] Blackwood J, Karczewski H, Huang MH, Pfalzer L. Katz activities of daily living disability in older cancer survivors by age, stage, and cancer type. Journal of Cancer Survivorship 2020;14:769–78.

[58] Braithwaite D, Satariano WA, Sternfeld B, Hiatt RA, Ganz PA, Kerlikowske K, Moore DH, Slattery ML, et al. Long-term prognostic role of functional limitations among women with breast cancer. JNCI: J Natl Cancer Inst 2010;102:1468–77.

[59] Brandberg Y, Johansson H, Hellstrom M, Gnant M, Mobus V, Greil R, Foukakis T, Bergh J. Long-term (up to 16 months) health-related quality of life after adjuvant tailored dose-dense chemotherapy vs. standard three-weekly chemotherapy in women with high-risk early breast cancer. Breast Cancer Res Treat 2020;181:87–96.

[60] Browall MM, Ahlberg KM, Persson LOG, Karlsson PO, Danielson EB. The impact of age on Health-Related Quality of Life (HRQoL) and symptoms among postmenopausal women with breast cancer receiving adjuvant chemotherapy. Acta Oncol 2008;47:207–15.

[61] Browall M, Ostlund U, Henoch I, Wengstrom Y. The course of Health Related Quality of Life in postmenopausal women with breast cancer from breast surgery and up to five years post-treatment. Breast 2013;22:952–7.

[62] Champion VL, Wagner LI, Monahan PO, Daggy J, Smith L, Cohee A, Ziner KW, Haase JE, et al. Comparison of younger and older breast cancer survivors and age-matched controls on specific and overall quality of life domains. Cancer 2014;120:2237–46.

[63] Clough-Gorr KM, Stuck AE, Thwin SS, Silliman RA. Older breast cancer survivors: geriatric assessment domains are associated with poor tolerance of treatment adverse effects and predict mortality over 7 years of follow-up. J Clin Oncol 2010;28:380–6.

[64] De Ligt KM, Heins M, Verloop J, Ezendam NPM, Smorenburg CH, Korevaar JC, Siesling S. The impact of health symptoms on health-related quality of life in early-stage breast cancer survivors. Breast Cancer Res Treat 2019;178:703–11.

[65] Dialla PO, Chu W-O, Roignot P, Bone-Lepinoy M-C, Poillot M-L, Coutant C, Arveux P, Dabakuyo-Yonli TS. Impact of age-related socio-economic and clinical determinants of quality of life among long-term breast cancer survivors. Maturitas 2015;81:362–70.

[66] Dubashi B, Vidhubala E, Cyriac S, Sagar T. Quality of life among young women with breast cancer: study from a tertiary cancer institute in South India. Indian J Cancer 2010;47:142–7.

[67] Enien M, Ibrahim N, Makar W, Darwish D, Gaber M. Health-related quality of life: impact of surgery and treatment modality in breast cancer. J Cancer Res Therapeut 2018;14:957–63.

[68] Extermann M, Leeuwenburgh C, Samiian L, Sehovic M, Xu J, Cubitt C, Jacobsen PB, Pahor M, et al. Impact of chemotherapy on medium-term physical function and activity of older breast cancer survivors, and associated biomarkers. Journal of Geriatric Oncology 2017;8:69–75.

[69] Girones R, Torregrosa D, Diaz-Beveridge R. Comorbidity, disability and geriatric syndromes in elderly breast cancer survivors. Results of a single-center experience. Crit Rev Oncol-Hematol 2010;73:236–45.

[70] Jayasinghe R, Fernando A, Jayarajah U, Seneviratne S. Post treatment quality of life among Sri Lankan women with breast cancer. BMC Cancer 2021;21(305). https://doi.org/10.1186/s12885-021-08055-5.

[71] Jones SM, Lacroix AZ, Li W, Zaslavsky O, Wassertheil-Smoller S, Weitlauf J, Brenes GA, Nassir R, et al. Depression and quality of life before and after breast cancer diagnosis in older women from the Women's Health Initiative. Journal of Cancer Survivorship 2015;9:620–9.

[72] Kamińska M, Ciszewski T, Kukiełka-Budny B, Kubiatowski T, Baczewska B, Makara-Studzinska M, Bojar I. Life quality of women with breast cancer after mastectomy or breast conserving therapy treated with adjuvant chemotherapy. Ann Agric Environ Med 2015;22:724–30.

[73] Karlsen RV, Frederiksen K, Larsen MB, Von Heymann-Horan AB, Appel CW, Christensen J, Tjonneland A, Ross L, et al. The impact of a breast cancer diagnosis on health-related quality of life. A prospective comparison among middle-aged to elderly women with and without breast cancer. Acta Oncol 2016;55:720–7.

[74] Klein D, Mercier M, Abeilard E, Puyraveau M, Danzon A, Dalstein V, Pozet A, Guizard AV, et al. Long-term quality of life after breast cancer: a French registry-based controlled study. Breast Cancer Res Treat 2011;129:125–34.

[75] Kornblith AB, Lan L, Archer L, Partridge A, Kimmick G, Hudis C, Winer E, Casey R, et al. Quality of life of older patients with early-stage breast cancer receiving adjuvant chemotherapy: a companion study to cancer and leukemia group B 49907. J Clin Oncol 2011;29:1022–8.

[76] Kostic S, Murtezani Z, Andric Z, Ivanovic N, Kozomara Z, Kostic M, Milicic V, Kocic S. Assessment of age-related influences on the quality of life of breast

cancer patients before and after surgical treatment. Vojnosanit Pregl 2020;77:908–16.
[77] Leinert E, Singer S, Janni W, Harbeck N, Weissenbacher T, Rack B, Augustin D, Wischnik A, et al. The impact of age on quality of life in breast cancer patients receiving adjuvant chemotherapy: a comparative analysis from the prospective multicenter randomized ADEBAR trial. Clin Breast Cancer 2017;17:100–6.
[78] Lemieux J, Brundage MD, Parulekar WR, Goss PE, Ingle JN, Pritchard KI, Celano P, Muss H, et al. Quality of life from Canadian cancer trials group MA.17R: a randomized trial of extending adjuvant letrozole to 10 years. J Clin Oncol 2018;36:563–71.
[79] Maharjan M, Thapa N, Adhikari RD, Petrini MA, Amatya KS. Quality of life of Nepalese women post mastectomy. Asian Pac J Cancer Prev APJCP: APJCP. 2018;19:1005–12.
[80] Mandelblatt JS, Makgoeng SB, Luta G, Hurria A, Kimmick G, Isaacs C, Tallarico M, Barry WT, et al. A planned, prospective comparison of short-term quality of life outcomes among older patients with breast cancer treated with standard chemotherapy in a randomized clinical trial vs. an observational study: CALGB #49907 and #369901. Journal of Geriatric Oncology 2013;4:353–61.
[81] Marinac C, Patterson RE, Villasenor A, Flatt SW, Pierce JP. Mechanisms of association between physical functioning and breast cancer mortality: evidence from the Women's Healthy Eating and Living Study. Journal of Cancer Survivorship 2014;8:402–9.
[82] Matalqah LM, Radaideh KM, Yusoff ZM, Awaisu A. Health-related quality of life using EQ-5D among breast cancer survivors in comparison with age-matched peers from the general population in the state of Penang, Malaysia. J Publ Health 2011;19:475–80.
[83] Maurer T, Thöne K, Obi N, Jung AY, Behrens S, Becher H, Chang-Claude J. Health-related quality of life in a cohort of breast cancer survivors over more than 10 years post-diagnosis and in comparison to a control cohort. Cancers 2021;13(8). https://doi.org/10.3390/cancers13081854.
[84] Michael YL, Wu C, Pan K, Seguin-Fowler RA, Garcia DO, Zaslavsky O, Chlebowski RT. Postmenopausal breast cancer and physical function change: a difference-in-differences analysis. J Am Geriatr Soc 2020;68:1029–36.
[85] Mosewich AD, Hadd V, Crocker PRE, Zumbo BD. Invariance testing of the SF-36 Health Survey in women breast cancer survivors: do personal and cancer-related variables influence the meaning of quality of life items? Soc Indicat Res 2013;110:559–77.
[86] Paskett ED, Alfano CM, Davidson MA, Andersen BL, Naughton MJ, Sherman A, Mcdonald PG, Hays J. Breast cancer survivors' health-related quality of life: racial differences and comparisons with noncancer controls. Cancer 2008;113:3222–30.
[87] Pires De Carvalho K, Miranda Lima MT, Mazzutti FS, Dias Custodio ID, Lajolo Canto PP, Paiva CE, Paiva Maia YCD. Longer times of receipt of adjuvant endocrine therapy correspond to improved functional capacity and lower adiposity in women receiving adjuvant therapy. Clin Breast Cancer 2019;19:e208–19.
[88] Quinten C, Kenis C, Hamaker M, Coolbrandt A, Brouwers B, Dal Lago L, Neven P, Vuylsteke P, et al. The effect of adjuvant chemotherapy on symptom burden and quality of life over time; a preliminary prospective observational study using individual data of patients aged ≥70 with early stage invasive breast cancer. Journal of Geriatric Oncology 2018;9:152–62.
[89] Sehl M, Lu X, Silliman R, Ganz PA. Decline in physical functioning in first 2 years after breast cancer diagnosis predicts 10-year survival in older women. Journal of Cancer Survivorship 2013;7:20–31.
[90] Sleight AG, Lyons KD, Vigen C, Macdonald H, Clark F. The association of health-related quality of life with unmet supportive care needs and sociodemographic factors in low-income Latina breast cancer survivors: a single-centre pilot study. Disabil Rehabil: An International, Multidisciplinary Journal 2019;41:3151–6.
[91] Wadasadawala T, Budrukkar A, Chopra S, Badwe R, Hawaldar R, Parmar V, Jalali R, Sarin R. Quality of life after accelerated partial breast irradiation in early breast cancer: matched pair analysis with protracted whole breast radiotherapy. Clin Oncol 2009;21:668–75.
[92] Williams LJ, Kunkler IH, King CC, Jack W, Van Der Pol M. A randomised controlled trial of post-operative radiotherapy following breast-conserving surgery in a minimum-risk population. Quality of life at 5 years in the PRIME trial. Health Technol Assess 2011;15:1–57.
[93] Xie X, Li H, Wang C, Li W, Xie D, Li M, Jiang D. Effect of modified radical mastectomy combined with neo-adjuvant chemotherapy on postoperative recurrence rate, negative emotion, and life quality of patients with breast cancer. Am J Tourism Res 2022;14(1):460–7.
[94] Young A, Weltzien E, Kwan M, Castillo A, Caan B, Kroenke CH. Pre- to post-diagnosis weight change and associations with physical functional limitations in breast cancer survivors. Journal of Cancer Survivorship 2014;8:539–47.
[95] Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85(5):365–76. https://doi.org/10.1093/jnci/85.5.365.
[96] Brooks RG, Jendteg S, Lindgren B, Persson U, Björk S. EuroQol: health-related quality of life measurement. Results of the Swedish questionnaire exercise. Health Pol 1991;18(1):37–48. https://doi.org/10.1016/0168-8510(91)90142-k.
[97] Brooks, R. with the EuroQol Group. EuroQol: the current state of play. Health Pol 1996;37(1):53–72.
[98] Ware J, Kosinski M, Keller S. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34(3):220–33.
[99] Jenkinson C, Wright L, Coulter A. Criterion validity and reliability of the SF-36 in a population sample. Qual Life Res 1994;3(1):7–12. https://doi.org/10.1007/BF00647843.
[100] Hays RD, Sherbourne CD, Mazel RM. User's manual for the medical outcomes study (MOS) core measures of health-related quality of life. Santa Monica, California: RAND Corporation, MR-162-RC; 1995. Available from: https://www.rand.org/pubs/monograph_reports/MR162.html. [Accessed 8 February 2021].
[101] Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23(2):137–45. https://doi.org/10.1002/art.1780230202.
[102] Nagi SZ. An epidemiology of disability among adults in the United States. Milbank Meml Fund Q - Health & Soc 1976;54(4):439–67.
[103] Hudak, P. L., Amadio, P. C., Bombardier, C. and The Upper Extremity Collaborative Group (UECG). Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. Am J Ind Med. 29(6), pp.602-608. doi: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4>3.0.CO;2-L.
[104] Jette AM, Branch LG. The Framingham Disability Study: II. Physical disability among the aging. Am J Publ Health 1981;71(11):1211–6.
[105] Taylor JO, Wallace RB, Ostfeld AM, Blazer DG. Established populations for epidemiologic studies of the elderly, 1981-1993: [East Boston, Massachusetts, Iowa and Washington Counties, Iowa, new haven, Connecticut, and North central North Carolina]. Inter-university Consortium for Political and Social Research 2006. https://doi.org/10.3886/ICPSR09915.v3. Available from: https://www.icpsr.umich.edu/web/NACDA/studies/9915/summary. [Accessed 13 December 2023].
[106] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The Index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914–9. https://doi.org/10.1001/jama.1963.03060120024016.
[107] Sprangers MAG, Groenvold M, Arraras JI, Franklin J, te Velde A, Muller M, Franzini L, Williams A, et al. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. J Clin Oncol 1996;14(10):2756–68.
[108] Postma TJ, Aaronson NK, Heimans JJ, Muller MJ, Hildebrand JG, Delattre JY, Hoang-Xuan K, Lantéri-Minet M, et al. The development of an EORTC quality of life questionnaire to assess chemotherapy-induced peripheral neuropathy: the QLQ-CIPN20. Eur J Cancer 2005;41(8):1135–9. https://doi.org/10.1016/j.ejca.2005.02.012.
[109] Khan F, Amatya B, Pallant JF, Rajapaksa I. Factors associated with long-term functional outcomes and psychological sequelae in women after breast cancer. Breast 2012;21:314–20. https://doi.org/10.1016/j.breast.2012.01.013.
[110] Capelan M, Battisti NML, McLoughlin A, Maidens V, Snuggs N, Slyk P, Peckitt C, Ring A. The prevalence of unmet needs in 625 women living beyond a diagnosis of early breast cancer. Br J Cancer 2017;117:1113–20. https://doi.org/10.1038/bjc.2017.283.
[111] World Health Organization. ICF checklist. Version 2.1a, clinician form. For International Classification of Functioning, Disability and Health. 2003. Available from: https://www.who.int/publications/m/item/icf-checklist. [Accessed 13 December 2023].
[112] Yang EJ, Kim B, Shin HI, Lim J. Use of the international classification of functioning, disability and health as a functional assessment tool for breast cancer survivors. Journal of Breast Cancer 2012;15(1):43–50. https://doi.org/10.4048/jbc.2012.15.1.43.
[113] Khan F, Amatya B, Ng L, Demetrios M, Pallant JF. Relevance and completeness of the International Classification of Functioning, Disability and Health (ICF) comprehensive breast cancer core set: the patient perspective in an Australian community cohort. J Rehabil Med 2012;44:570–80. https://doi.org/10.2340/16501977-0972.
[114] Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ulf E, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35(8):1381–95. https://doi.org/10.1249/01.MSS.0000078924.61453.FB.
[115] Kwan W, Jackson J, Weir LM, Dingee C, McGregor G, Olivotto IA. Chronic arm morbidity after curative breast cancer treatment: prevalence and impact on quality of life. J Clin Oncol 2002;20(20):4242–8. https://doi.org/10.1200/JCO.2002.09.018.
[116] Gordon NH, Siminoff LA. Measuring quality of life of long-term breast cancer survivors: the long term quality of life–breast cancer (LTQOL-BC) scale. J Psychosoc Oncol 2010;28(6):589–609. https://doi.org/10.1080/07347332.2010.516806.
[117] Fortner B, Okon T, Schwartzberg L, Tauer K, Houts AC. The cancer care monitor: psychometric content evaluation and pilot testing of a computer administered system for symptom screening and quality of life in adult cancer patients. J Pain Symptom Manag 2003;26(6):1077–92. https://doi.org/10.1016/j.jpainsymman.2003.04.003.
[118] Misajon R, Pallant JF, Manderson L, Chirawatkul S. Measuring the impact of health problems among adults with limited mobility in Thailand: further validation of the Perceived Impact of Problem Profile. Health Qual Life Outcome 2008;6(6). https://doi.org/10.1186/1477-7525-6-6.
[119] Devoogdt N, Van Kampen M, Christians MR, Troosters T, Piot W, Beets N, Nys S, Gosselink R. Short- and long-term recovery of upper limb function after axillary lymph node dissection. Eur J Cancer Care 2011;20:77–86. https://doi.org/10.1111/j.1365-2354.2009.01141.x.

[120] Beaton DE, Wright JG, Katz JN, The Upper Extremity Collaborative Group. Development of the QuickDASH: comparison of three item-reduction approaches. J Bone Joint Surg 2005;87-A(5):1038–46.
[121] L'Insalata JC, Warren RF, Cohen SB, Altchek DW, Peterson MGE. A self-administered questionnaire for assessment of symptoms and function of the shoulder. J Bone Joint Surg 1997;79-A(5):738–48.
[122] World Health Organization. WHOQOL-BREF: introduction, administration, scoring and generic version of the assessment. Field Trial Version. Switzerland: Programme on Mental Health: Geneva; 1996. Available from: https://www.who.int/publications/i/item/WHOQOL-BREF. [Accessed 13 December 2023].
[123] Dahl AA, Nesvold IL, Reinertsen KV, Fossa SD. Arm/shoulder problems and insomnia symptoms in breast cancer survivors: cross-sectional, controlled and longitudinal observations. Sleep Med 2011;12:584–90.
[124] Blackwood J, Rybicki K. Physical function measurement in older long-term cancer survivors. Journal of Frailty, Sarcopenia and Falls 2021;6:139–46. https://doi.org/10.22540/JFSF-06-139.
[125] Young T, Velikova G, et al. EORTC QLQ-C30 normative data for the United Kingdom: results of a cross-sectional survey of the general population. Eur J Cancer 2024. https://doi.org/10.1016/j.ejca.2024.113927.
[126] Ashwini K. Wearable sensor technology to measure physical activity (PA) in the elderly. Current Geriatrics Report 2019;8:55–66. https://doi.org/10.1007/s13670-019-0275-3.
[127] Keogh A, Taraldsen K, Caulfield B, Vereijken B. It's not about the capture, it's about what we can learn": a qualitative study of experts' opinions and experiences regarding the use of wearable sensors to measure gait and physical activity. J NeuroEng Rehabil 2021;18:78. https://doi.org/10.1186/s12984-021-00874-8.
[128] Petersen M, Vachon H, et al. Development of standard computerised adaptive test (CAT) settings for the EORTC CAT Core. Qual Life Res 2014;33:951–61. https://doi.org/10.1007/s11136-023-03576-x.
[129] Brodke D, Goz V, et al. PROMIS® PF CAT outperforms the ODI and SF-36 physical function domain in spine patients. Spine.15 2017;42(12):921–9. https://doi.org/10.1097/BRS0000000000001965.
[130] Bedard G, Zeng L, et al. Minimal important differences in the EORTC QLQ-C30 in patients with advanced cancer. Asia Pac J Clin Oncol 2014;10:109–17. 10.111/ajco.12070.
[131] Musoro J, Coens C, et al. Minimally important differences for interpreting EORTC QLQ-C30 scores in patients with advanced breast cancer. JNCI Cancer Spectr 2019. https://doi.org/10.1093/jncics/pkz037.
[132] Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A, on behalf of the EORTC Quality of Life Group. The EORTC QLQ-C30 scoring manual. third ed. Brussles: European Organisation for Research and Treatment of Cancer; 2001.
[133] Vanier, A., Oort, F. J., McClimans, L., Ow, N., Gulek, B. G., Böhnke, J. R., Sprangers, M., Sébille, V. et al. The Response Shift - in Sync Working Group. 2021. Response shift in patient-reported outcomes: definition, theory, and a revised model. Qual Life Res. 30(12), pp.3309-3322. doi: 10.1007/s11136-021-02846-w.
[134] McMillan. Available from: Breast Cancer 2018. https://www.macmillan.org.uk/cancer-information-and-support/breast-cancer#after_treatment. [Accessed 9 February 2021].
[135] Levangie PK, Drouin J. Magnitude of late effects of breast cancer treatments on shoulder function: a systematic review. Breast Cancer Res Treat 2009;116(1):1–15. https://doi.org/10.1007/s10549-008-0246-4.