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Research Article

Translating Evidence from Dutch Exercise Oncology Trials in Patients with Breast Cancer into Clinical Practice Using the RE-AIM Framework

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Purpose. We aimed to evaluate the potential for implementing exercise interventions for patients with breast cancer in the Netherlands, based on findings of the Dutch randomized controlled trials in this population. *Methods*. We evaluated the implementation of four Dutch exercise trials retrospectively, using the five dimensions of the RE-AIM framework: Reach (exercise participation rate), Effectiveness for physical fitness, fatigue, quality of life, and physical function, Adoption (e.g., satisfaction of physical therapists guiding the exercise intervention), Implementation (cost-effectiveness and exercise adherence correlates thereof), and Maintenance (maintenance of exercise levels by individual patients and sustainability of exercise delivery at organization level). Thereby, we reflect on these results using (international) literature to gain better insight in overall barriers, facilitators, and opportunities for further implementation of exercise interventions. *Results*. Participation rates of 44–52% not only indicated acceptable Reach in the context of a trial but also indicated room for improvement. Effectiveness of exercise during and after treatment was demonstrated in most trials showing benefits for aerobic fitness, physical fatigue, quality of life and physical function, and high patient satisfaction. Adoption of the exercise interventions by physical therapists was adequate (satisfaction score: 7.5 out of 10). Evaluation of Implementation indicated adequate adherence to supervised exercise, inconsistent findings on potential correlates of adherence, and promising results on cost-effectiveness. Currently, reimbursement for exercise programs is lacking. Maintenance of intervention effects at the patient level was limited and inconsistent. Maintenance of intervention availability at the organizational level was facilitated by an extensive network of specially trained physical therapists, but better communication and collaboration between different healthcare professionals are desired. *Conclusions*. Improved implementation could particularly be achieved by increasing reach and improved focus on exercise maintenance on both the patient and organizational level.

1. Introduction

Evidence from randomized controlled trials (RCTs) indicates that exercise benefits aerobic fitness [1], fatigue [2], health-related quality of life (HRQoL) [3], and physical function [3, 4], during and after cancer treatment. This has led to the development of national and international guidelines [5–9] recommending exercise as an integral part of cancer care in a number of countries and professions, including sports medicine [4], medical oncology [10], and physical therapy [11, 12]. However, widespread implementation of exercise interventions is still limited. Translating research from RCTs into practice has shown to be difficult because of problems with population representativeness, limited (financial) resources, and program availability and sustainability [13].

In 1999, the RE-AIM framework was developed to evaluate the potential for dissemination of research into clinical practice and to facilitate this process [14]. Since then, RE-AIM has been used to plan, evaluate, and review health promotion and disease management interventions [14, 15]. In the RE-AIM framework, the overall impact of an intervention is described in five dimensions: reach, effectiveness, adoption, implementation, and maintenance (Table 1).

Over the past years, four exercise RCTs have been conducted in the Netherlands that evaluate the effect of supervised exercise interventions on aerobic fitness or fatigue as primary endpoint in patients with breast cancer during treatment (physical activity during cancer treatment (PACT) [16–21] and physical exercise during adjuvant chemotherapy effectiveness study (PACES) [22–26]) and after treatment (resistance and endurance exercise after chemotherapy (REACT) [27–30] and UMBRELLA Fit [31, 32]) (Table 2).

In this study, we aimed to evaluate the potential for implementation of exercise interventions for people who have been treated for breast cancer with curative intent, based on these four RCTs, with the use of the RE-AIM framework. We summarize the findings from the four Dutch trials only, since implementation of interventions is a dynamic, context-specific process [33], with (country) specific and more generalizable components. In addition, we reflect on these results using (international) literature (e.g., trials and reviews) to gain better insight in overall barriers and facilitators for the implementation of exercise interventions. Finally, we describe opportunities for further optimization of implementation.

2. Methods

For each dimension of the RE-AIM model, we summarized the findings from the four Dutch trials, as published before August 2022, using the operationalizations of reach, effectiveness, adoption, implementation, and maintenance described in Table 1. Most results have been published previously [17, 19, 20, 22, 23, 25, 26, 32], except for information on patient satisfaction (PACT and UMBRELLA Fit trial). As the REACT trial also included patients with other types of cancer, we performed subgroup analyses on the subpopulation of patients with breast cancer, except for the cost-effectiveness analyses of which results are presented from the original papers. For better comparisons, we calculated Cohen's d effect sizes (ES) of the intervention effects, where significant effects ($p \leq 0.05$) were considered as no substantial difference for ES ≤ 0.2, small for ES 0.2–0.5, moderate for ES 0.5–0.8, and large for ES ≥ 0.8 [34].

3. Results

3.1. Reach

3.1.1. Summary of Results of Dutch RCTs. Across the four RCTs, 44–52% of eligible patients were willing to participate in the trials and the exercise intervention. Main reasons for nonparticipation were lack of time, mental burden, travel distance to the hospital, not wanting to be randomized, or wanting to exercise on their own (Table 3).

Comparison of participants and nonparticipants indicated that patients with a higher educational level were more likely to participate in exercise trials both during and after treatment (Table 3). Additionally, behavioral motivational factors were associated with participation during chemotherapy. Patients with more expected benefits of exercise, higher self-efficacy, fewer negative attitudes, more social support, and fewer perceived barriers to exercise were more likely to participate. Conversely, for exercise interventions following completion of anticancer treatment, patients who perceived more barriers were more likely to participate (Table 3).

3.1.2. Reflections and Opportunities to Improve Implementation. The reported participation rate of 44–52% in the Dutch exercise trials is somewhat higher than the pooled estimate of 30% reported in a meta-analysis of 23 exercise trials in patients with breast cancer [35]. The highest participation rate of 52%, reported by the UMBRELLA Fit trial, is likely related to the trials within cohorts (TwiCs) design, in which patients participating in an observational cohort were randomly invited to participate in an exercise intervention, thereby limiting intervention nonparticipation due to unwillingness to be randomized [31, 36]. In other trials, this proportion was shown to be approximately 10–15% [17, 26] (Table 3). Additionally, participation rates were influenced to some extent by the eligibility criteria employed, as they most often excluded patients with severe comorbidities and those with cognitive disorders or not fluent in Dutch. These patients may benefit even more from exercise guidance, as they may need specific exercise prescriptions, and may be less aware of health benefits and less able to find adequate health information, respectively. Patients with insufficient mastery of the language may benefit from additional health communication strategies, such as including visual aids to improve reach [37, 38].

Table 1: Definitions of the RE-AIM framework and operationalization used in the current study.

Reach	Refers to the number and characteristics of participants when compared to the target audience Operationalization: reach was evaluated by the number and characteristics of participants included in the exercise trials when compared to the target population
Effectiveness	Refers to the positive and negative consequences of the intervention under optimal conditions or real-world circumstances, respectively Operationalization: effectiveness was evaluated by the impact of an intervention on aerobic fitness, fatigue, quality of life, self-reported physical function, and patient satisfaction
Adoption	Refers to the staff and settings that participate Operationalization: adoption was evaluated as the representativeness of settings and satisfaction of staff involved in the Dutch exercise trials
Implementation	Refers to the extent to which the program was implemented as intended, i.e., intervention fidelity and resources (e.g., cost and time) Operationalization: implementation was evaluated by (i) the participants' adherence to an exercise program and (ii) resources and intervention costs
Maintenance	Refers to the long-term effects, both at the level of the individual patient and at the level of the organization in terms of the sustainability of the program delivery over time in the settings without added resources and leadership Operationalization: we describe maintenance at both the patient (individual) and setting level. At the patient level, maintenance has been defined as the long-term effects (≥6 months) of the intervention. At the setting level, we examined the extent to which the exercise programs are institutionalized or part of the routine organizational practices and policies

The finding that travel time to the hospital was a commonly reported barrier to exercise participation is in line with other studies reporting that cancer survivors rated long travel time to exercise facilities as an important barrier to participation, particularly when supervised sessions were scheduled for 2 or 3 times per week [39, 40]. Travel time can be reduced by offering exercise interventions in local physical therapy practices or in the community settings close to patients' homes. In the Netherlands, regional networks of physical therapists working with patients with cancer are expanding, facilitating the accessibility to supervised exercise sessions. In addition, a network of fitness instructors with additional oncology education is developing, which might ease the transition from healthcare to community settings.

Experiencing less "barriers to exercise" was associated with higher participation during chemotherapy, while, after treatment, patients with more barriers were more likely to participate. These findings might indicate that at start of treatment, patients might be too occupied with the burden of diagnosis and treatment to overcome existing barriers to exercise, while, after treatment, patients' declined fitness levels and difficulties overcoming these might make them more prone to accept exercise guidance.

Two other commonly reported barriers are time and mental burden (e.g., "having too many things on one's mind") [41]. In studies with patients under active treatment, the timing of trial inclusion before the start of chemotherapy is challenging because of the short time window between diagnosis and start of treatment and because patients who were diagnosed recently can be overwhelmed [26]. These barriers might be reduced by improving knowledge on the content and benefits of exercise during and after chemotherapy and by optimizing the timing of discussing exercise with patients. Shaping knowledge is among the most commonly used behavioral change techniques [42]. Specifically, instructions on how to perform the exercise behavior and information on the health consequences thereof were often part of interventions that were effective in improving exercise behavior in breast cancer survivors [43]. Hence, increasing knowledge of health benefits may help patients to restructure priorities. This may also be the case for patients with lower educational levels, who were less willing to participate in exercise trials both during and after chemotherapy [26, 30]. However, for the latter patients, the educational techniques applied might need to be adapted, for example, by breaking down information into small concrete steps and/or by including visual aids [37].

In the Netherlands, an e-learning module is available for nurse (practitioners), which, in addition to addressing common effects of exercise in patients with cancer, also pays attention to how to coach and motivate patients towards improving and maintaining adequate exercise levels [44]. The optimal timing of discussing exercise with patients is unknown while results from the Dutch trials indicated that thinking about exercise shortly after diagnosis may be an additional burden for some patients; for other patients, the diagnosis may be a teachable moment [45] and the right time to discuss exercise at the time of diagnosis [46]. It is also likely that patients' information needs and receptivity change over the course of their treatment and recovery although this is currently an understudied subject. The ACSM's Exercise Is Medicine (EIM) initiative proposes assessing, advising, and referring to physical activity in a recurrent pattern to take into account the different preferences and changing needs of patients for referral to

Table 2: Characteristics of the studies.

	No.	Study arms	Mean age (SD)	Timing of the intervention and duration	Description of the intervention (FITT)[a]
PACT–breast cancer [17, 18]	204	Intervention ($n = 102$) Control (usual care) ($n = 102$)	Intervention: 49.7 (8.2) Control: 49.5 (7.9)	During chemotherapy and/or radiotherapy Duration = 18 weeks	F: 2x/week I: (i) AE: HR at or below VT (ii) RE: 65% of 1RM (2 × 10) towards 45% of 1RM (2 × 20) T: 60 min T: (i) AE: interval training of alternating intensity (25 min) (ii) RE: major muscle groups (25 min)
PACES-breast cancer [23, 24]	230	OnTrack ($n = 76$) supervised exercise program Onco-move ($n = 77$) home-based, individualized, self-managed PA program Control (usual care) ($n = 77$)	OnTrack: 49.8 (8.4) Onco-move: 50.5 (10.1) Usual care: 51.6 (8.8)	During chemotherapy Duration = start in week of first chemotherapy cycle until 3 weeks after the last cycle of chemotherapy (mean = 118.6 days of length of chemotherapy)	*OnTrack* F: 2x/week I: (i) AE: 50–80% of Wmax as estimated by SRT (ii) RE: 70% of 1RM (2 × 12) towards 80% of 1 RM (2 × 8) T: 60 min T: (i) AE: min. Duration of 10 min per exercise (total 30 min) (ii) RE: ≥6 exercises of major muscle groups (20 min) *Onco-move* F: 1x/3 weeks + 2 weeks after start (per telephone) I: moderate intensity–Borg 12–14 T: 30 min per day T: activities depend on patient preference
UMBRELLA Fit [31, 32]	260 (TwiCs design; $n = 68$ accepted the intervention)	Intervention ($n = 130$) Control (usual care) ($n = 130$)	Intervention: 58.0 (9.8) Control: 58.3 (9.5)	After cancer treatment (except for hormonal therapy) Duration = 12 weeks	F: 2x/week I: (i) AE: week 1–3: 40-6-%% HRR + HRrest week 4–8: 60–70% HRR + HRrest; week 9–12 : 60–75% HRR + HRrest + interval-training (ii) RE: week 1–3: 1 × 20–25rep (20RM) 9 exercises week 4–12: 2 × 15–20 rep (15RM) 7 exercises T: 60 min T: (i) AE: gradually increase, week 1–3: 15–20 min week 4–8: 15–20 min MI & 5–10 min HI week 9–12 : 10 min moderate intensity & 10 min HIIT, 10 × 30 sec, 1 min active rest (ii) RE: major muscle groups

Table 2: Continued.

	No.	Study arms	Mean age (SD)	Timing of the intervention and duration	Description of the intervention (FITT)[a]
REACT [27, 28]	181 Breast	HI ($n = 62$) LMI ($n = 62$) WLC ($n = 57$)	HI: 51.7 (9.5) LMI: 51.8 (10.5) WLC: 51.9 (8.2)	After chemotherapy Duration = 12 weeks	*HI* F: 2x/week I: (i)AE: first 4 weeks 2 × 8 min with alternating workloads (ii) (30/65% MSEC) after 4 weeks 1 × 8 min interval (iii) Supplemented with 3 × 5 min constant workload (iv) (≥80% HRR) (v) RE: 70% 1RM (2 × 10) to 85% 1RM (2 × 10) T: 60 min T: (i) AE: two types of endurance interval exercises (ii) (week 1–4: 16 min week ≥ week 5 : 25 min) (iii) RE: 6 exercises of major muscle groups (25 min) *LMI*: F: 2x/week I: (i) AE: first 4 weeks 2 × 8 min with alternating workloads (ii) (40/55% MSEC) after 4 weeks 1 × 8 min interval (iii) supplemented with 3 × 5 min constant workload (iv) (40–50% HRR) (v) RE: 40% 1RM (2 × 10) to 55% 1RM (2 × 10) T: 60 min T: (i)AE: two types of endurance interval exercises (ii) (week 1–4: 16 min week ≥ week 5 : 25 min) (iii) RE: 6 exercises of major muscle groups (25 min)

[a]Complementary to the supervised interventions, participants were encouraged to be physically active at moderate intensity for at least 30 minutes, 3–5 times per week in all trials. *1RM*: one-repetition maximum; *AE*: aerobic exercise; *FITT*: frequency intensity time type; *HI*: high intensity; *HIIT*: high intensity interval training; *HR*: heart rate; *HRR*: heart rate reserve; *HRrest*: resting heart rate; *LMI*: low-to-moderate intensity; *PACES*: physical exercise during adjuvant chemotherapy effectiveness study; *PACT*: physical activity during cancer treatment; *MI*: moderate intensity; *MSEC*: maximal short exercise capacity; *RE*: resistance exercise; *REACT*: resistance and endurance exercise after chemotherapy; *RM*: repetition maximum; *SD*: standard deviation; *SRT*: steep ramp test; *TwiCs*: trials within cohorts; *UMBRELLA Fit*: utrecht cohort for multiple breast cancer intervention studies and long-term evaluation; *VT*: ventilatory threshold; *WLC*: wait list control; *Wmax*: maximal wattage.

exercise programs [47]. For trial purposes, with small windows of opportunity for including patients at the start of chemotherapy, an improvement in research infrastructure and a proactive approach to patients would be helpful, e.g., an outpatient research clinic, where patients are being asked at diagnosis for a broad consent for being approached for (future) research participation. Broad consent enables researchers to directly approach patients without intercession of a healthcare provider and outside a medical appointment.

Physicians play an important role in referring patients to exercise, and thus, in increasing the reach, as patients are more likely to participate in exercise, it has been recommended by a physician [40, 48, 49]. However, while most oncologists, including those in the Netherlands, report understanding the importance of exercise, only one in three actually refers patients [50–52]. Reported barriers for this poor referral rate are lack of time, insufficient knowledge, and safety concerns [53]. It has been suggested that the development of a roadmap for oncology clinicians with detailed pathways for exercise programming, in which discussing exercise participation becomes part of routine care, would facilitate referral [47]. However, empirical evidence on the effectiveness of such a roadmap and feasibility in Dutch clinical practice is lacking. Additionally, physicians' referral may also be improved by increasing patient awareness of exercise benefits, empowering patients to raise the issue of referral themselves during consultation [54], and improving insurance reimbursement and thereby accessibility [52].

3.2. Effectiveness

3.2.1. Summary of Results of Dutch RCTs. Supervised exercise interventions *during* chemotherapy had a significant positive effect on aerobic fitness in one study [23], but it was not statistically significant in the other [17]. Supervised exercise limited physical fatigue significantly, while an unsupervised exercise program did not (Table 3). Both supervised and unsupervised exercise had a significant beneficial effect on physical functioning in one trial [23] but not in the other [17] (Table 3).

Exercise *after* completion of treatment significantly improved aerobic fitness, physical functioning, global QoL, and general fatigue in one trial (Table 3) and physical fatigue in both trials [32] (Table 3).

Average patient satisfaction was 8.5 (on a 1–10 scale) for supervised exercise *during* chemotherapy, 8.4 for supervised exercise *after* treatment, and 7.4 for an unsupervised exercise program *during* chemotherapy. Up to 25% of patients reported that the exercise program *during* chemotherapy was "too burdensome." After treatment, up to 16% of patients reported the program as "not being tailored enough," up to 10% reported difficulties with scheduling exercise sessions, and some patients reported the exercise program as "(too) heavy or exhausting" (12% up to 17% for patients in the High Intensity (HI) exercise group) (Table 3).

3.2.2. Reflections and Opportunities for Further Implementation. The beneficial effects of exercise on aerobic fitness, fatigue, and HRQoL found in the Dutch trials correspond with findings from other studies [4]. Of note, the stringent eligibility criteria of RCTs (e.g., excluding patients with serious orthopedic and cardiovascular or pulmonary comorbidities) may hamper generalizability of the beneficial effects to all patients with breast cancer treated with curative intent. Although it may be expected that these patients could also benefit from exercise, more extensive tailoring of the exercise protocols is likely necessary to take specific comorbidities into consideration [55].

The beneficial effects on aerobic fitness, fatigue, and HRQoL, both during and after treatment, were also reported by several meta-analyses on aggregated and individual patient data (IPD) meta-analyses [1–3] that also reported larger benefits for supervised interventions and patients with lower baseline HRQoL [56]. High baseline values of HRQoL may explain the lack of effects on HRQoL in the UMBRELLA Fit trial as the HRQoL in this cohort of patients was already comparable to the Dutch general female population at the start of the intervention, leaving little room for improvement [32].

The average effects of exercise on aerobic fitness observed in the Dutch trials correspond to the mean peakVO_2 improvements of 1.80 and 2.13 ml/kg/min reported in the literature [57]. Strikingly, previous studies with IPD analyses reported that exercise interventions during treatment did not yield benefits for aerobic fitness in patients with a low fitness level (peakVO_2 below 15.4 ml/kg/min, which is the threshold for functional independence in women [58]) at baseline [56]. Also, effects on aerobic fitness were smaller in older patients [1]. The limited effects in these subgroups may be related to low adherence or inability to complete exercises as intended and highlight the need for exercise interventions that are specifically tailored to older and unfit cancer patients to further improve implementation.

The Dutch trial results suggest a dose-response effect for exercise intensity on aerobic fitness (low-to-moderate (LMI) versus HI) (Table 3). Internationally, in the past 5 years, an increasing number of studies successfully examined the effects of high intensity interval training (HIIT) in patients with cancer and found positive results on cardiorespiratory fitness and cancer-related fatigue [59, 60]. However, results of the Dutch trials suggest that HIIT may not be the best choice for all patients, as up to one quarter of the patients indicated that the exercise intervention conducted during cancer treatment was too burdensome directly after their chemotherapy administration, and 17% of those who participated in HI exercise after cancer treatment found it (too) heavy or exhausting (Table 3). Also, depending on the goal of the intervention, higher exercise intensity may not always be necessary. For example, relatively low volumes of resistance exercises, at moderate-to-high intensity, have been found to yield significant benefits in terms of fatigue levels and HRQoL in patients with prostate cancer [61].

Despite the finding that some patients found the intervention to be too strenuous or burdensome, the vast majority of the patients in the four Dutch trials indicated being very satisfied with the exercise interventions in which they participated. This has also been the case in other exercise trials in patients with breast cancer [62–64]. Patients

Table 3: Results of the Dutch exercise trials summarized using the dimensions of the RE-AIM framework.

Reach					
	During chemotherapy [17, 26]		After treatment [30, 32][a]		
Recruitment setting	Both academic and general hospitals		Both academic and general hospitals		
Inclusion and exclusion criteria	Histologically diagnosed breast cancer <6–10 weeks before recruitment; stage M0; scheduled for chemotherapy; aged 25–75 years (PACT)/aged >18 years (PACES); Karnofsky performance status ≥60; no contraindications for physical activity; no cardiovascular, serious orthopedic, or cardiopulmonary conditions; no malnutrition; basic fluency in Dutch language; no psychiatric or cognitive problems		Histologically diagnosed breast cancer; completed (neo)adjuvant chemotherapy; no contraindications for exercise; able to perform basic activities; no psychiatric or cognitive problems; basic fluency of Dutch language		
Participation rate	44% and 48%		47% and 52%[b]		
Barriers to participation	Time/mental burden (34–40%); travel distance to hospital (12–22%); problem with random assignment (11–15%); want to exercise by him-/herself (24%); poor timing (22%); does not want to exercise (18%); unknown (1–23%)		Mental burden (26–55%); not interested/did not want to exercise (8–19%); already exercising (17–23%); problem with randomization (10%); unknown (8–21%)		
Characteristic participants versus nonparticipants[c] Characteristic participants versus nonparticipants[d]	Higher educational level, more likely to be employed, less fatigue, higher HRQoL, higher self-efficacy, fewer negative attitudes, more social support, more benefits and fewer barriers, lower self-reported activity level; lower cancer stage (I-II); less likely to have had a mastectomy More likely to be employed, lower self-reported activity level, lower exercise stage (maintenance); more social support; fewer negative attitudes		[e]Higher educational level, younger, lower BMI, higher outcome expectations, lower distress, more barriers		
Effectiveness					
	During chemotherapy [17, 23] Effect sizes[f]		After treatment [28, 32][a] Effect sizes		
General fatigue	Supervised Unsupervised	0.23 and 0.29 0.17	MHI vs control 0.09	LMI vs WLC 0.40	HI vs WLC 0.43
Physical fatigue	Supervised Unsupervised	0.30 and 0.63 0.28	MHI vs control 0.24	LMI vs WLC 0.40	HI vs WLC 0.64
Aerobic fitness[g]	Supervised Unsupervised	0.11 and 0.45 0.14	NA	LMI vs WLC 0.21	HI vs WLC 0.35
Left knee extensor peak torque[h]	Supervised	0.33	NA		
HHD (knee extensor)[i]	Supervised Unsupervised	0.38 0.10	NA		
HHD (elbow flexion)[i]	Supervised Unsupervised	0.54 0.21	NA		
Quality of life	Supervised Unsupervised	0.11 and 0.28 0.25	MHI vs control 0.05	LMI vs WLC 0.27	HI vs WLC 0.54
Self-reported physical functioning	Supervised Unsupervised	0.16 and 0.81 0.68	MHI vs control 0.02*	LMI vs WLC 0.28	HI vs WLC 0.27

Table 3: Continued.

	Patient satisfaction during chemotherapy [22][j]	Patient satisfaction after treatment[a,k]
Patient satisfaction with supervised exercise program[l]	*Average scores*: 8.5 out of 10 on overall satisfaction with the exercise program 9.4 out of 10 on "would you recommend this program to fellow patients?" *Experiences (positive)*: (i) Benefits (better physical fitness, positive feelings, more energy, fulfilment, better appetite and confidence in and positivity about the body) (44%) (ii) Good timing of the exercise intervention (63–91%) (iii) Intensity and load of the program overall (90%) *Experiences (negative or suggestions)*: (i) Intervention was burdensome (burdensome directly after chemotherapy or when ill) (4–25%) (ii) Inadequate supervision (e.g., no discussion of the diary and lack of continuity of supervision) (20%) (iii) Difficulty with scheduling (16–18%) (iv) More variation in training (by adding, for example, yoga or aerobics and more personalized supervision) (45%) (v) Total duration of intervention period too short (32%)	*Average score*: 8.4 out of 10 on overall satisfaction with the exercise program *Experiences (positive)*: (i) Improvement in physical fitness (LMI: 20%, MHI: 28%, and HI: 26%) (ii) Guidance by the physical therapist with regard to the supervised exercises (LMI: 21%, MHI: 23%, and HI: 21%) (iii) Exercising with peers (LMI: 12%, MHI: 3%, and HI: 9%) *Experiences (negative or suggestions)*: (i) Training (too) heavy or (too) exhausting (LMI: 2%, MHI: 12%, and HI: 17%) (ii) Difficulty with scheduling (LMI: 8%, MHI: 10%, HI: 10%) (iii) The program as not being tailored enough (LMI: 6%, MHI: 16%, and HI: 10%) (iv) Improved variation in exercises and/or less arm exercises (LMI: 7%, MHI: 26%, and HI: 5%)
Patient satisfaction with unsupervised exercise program[l]	*Average scores*: 7.4 out of 10 on overall satisfaction 8.2 out of 10 on "would you recommend this program to fellow patients?" *Experiences (positive)*: (i) Structure on how to be physically active (38%) (ii) Benefits (physical fitness gave less stress and fatigue and made them feel better and happier) (29%) *Experiences (negative)*: (i) Limited counseling (42%) (ii) The diary is burdensome (19%)	NA
Adoption		
Guidance of the exercise programs	(i) Patients in the Dutch RCTs were referred to a trained PT close to their home to guide the exercise intervention. The PTs were trained on the specific exercise protocols by the coordinating researcher before the start of the intervention (ii) In the Netherlands, PTs are the exercise professionals whom are dedicated to supervise the exercise programs for patients during chemotherapy	
Satisfaction of physical therapists[l]	(i) 20 PTs rated the exercise intervention after chemotherapy with a 7.5 out of 10 (ii) Preference for HI over LMI, but with the suggestion to start with LMI in patients with reduced physical fitness (iii) Preference for a more flexible exercise protocol to be able to improve variation of exercises (iv) Counseling techniques were rated with a 7 out of 10, with remarks that the counseling was not always possible in the available time (20%) and PTs expressed a need for education with regard to counseling techniques (10%)[l]	

Table 3: Continued.

Implementation–participants adherence							
	During chemotherapy [17, 22]				After treatment [30, 32][a]		
Attendance[n] median% (IQR%)	Supervised	77 [35–60] and 83 [39–61]			MHI	LMI	HI
	Unsupervised	71 [35–53, 62–77]			96 (88–100)	88 [37–61, 78–82]	92 [50–61, 78–82]
Compliance[o] median% (IQR%)	Aerobic	Duration[q] 88 [35–61, 76–83]	Intensity[r] 50 (22–82)	Advice 61 (33–79)	NA	LMI 81 [38–61, 78]	HI 88 [43–61, 78–81]
	Resistance	84 [35–61, 78–80]			NA	LMI 92 [55–61, 78–82]	HI 94 (88–98)
Predictors of high attendance[a,n,p]	Supervised	Higher educational level, low BMI, higher disease stage, having a partner			NA	LMI Treatment with hormonal therapy	HI Sport history, higher exercise stage, radiotherapy, higher self-efficacy, positive attitude, less barriers
	Unsupervised	Higher baseline endurance time, attitude					
	Exercise advice	Higher baseline fitness (endurance time)					
Predictors of high compliance[a,o,p]	Aerobic	Duration: No significant predictors	Intensity: Low levels of baseline physical fatigue; no addition of radiotherapy to chemotherapy		NA	LMI No employment at baseline	HI Higher self-efficacy and positive attitude
	Resistance	Her2+ and ER or PR + tumor type (vs. triple negative); lower BMI; lower baseline PA			NA	LMI No employment at baseline and lower education	HI Having a more positive attitude towards exercise
	Exercise advice	Beliefs about PA; higher baseline PA; peak O_2 consumption					
Implementation–cost-effectiveness							
Currently, physical therapy is not reimbursed through basic healthcare insurance in the Netherlands. For patients who have been hospitalized prior to their chemotherapy or had radiotherapy sessions in the past 6 months, physical therapy is covered starting from the 21st session. Hence, patients who receive neoadjuvant chemotherapy are not entitled to any reimbursement from basic coverage, and patients who receive adjuvant chemotherapy face out-of-pocket expenses for the first 20 sessions, unless they have additional coverage packages							
During chemotherapy [21, 25]					After treatment [29]		
Supervised	(i) The OnTrack intervention (PACES trial) was found to be cost-effective for QALYs Mean intervention costs for the supervised intervention were 756.67 euros per participant. The probability of OnTrack being cost-effective compared with UC was 45% at a willingness-to-pay of 20.000€/QALY and 79% at a willingness-to-pay of €80.000/QALY (ii) The probability that the PACT intervention is cost-effective for patients with breast cancer is 2% for a willingness-to-pay 20.000/QALY and 6% for a willingness-to-pay €80.000/QALY				(i) The probability that HI was cost-effective compared to LMI exercise was 0.91 at 20.000€/QALY and 0.95 at 52.000€/QALY		
Unsupervised	(i) The unsupervised OncoMove intervention (PACES trial) was found not to be cost-effective (ii) Mean intervention costs for the unsupervised intervention were 46 euros per participant. The probability of cost-effectiveness was 25% at a willingness-to-pay of 20.000€/QALY and 55% at a willingness-to-pay of €80.000/QALY						

Table 3: Continued.

Maintenance–patient level					
	During chemotherapy [19, 23]				After treatment [29][a]
		6 months	8 months	48 months	15 months (HI vs LMI)
	Effect sizes				Effect sizes
General fatigue	Supervised Unsupervised	0.28 0.16	0.22 NA	0.04 NA	0.06
Physical fatigue	Supervised Unsupervised	0.18 0.01*	0.11 NA	0.17 NA	0.17
Aerobic fitness[g]	Supervised Unsupervised	0.13 0.08	0.10* NA	NA	0.21
Left knee extensor peak torque[h]	Supervised	NA	0.20	NA	NA
HDD (knee extensor)[i]	Supervised Unsupervised	0.06 0.02	NA	NA	NA
HHD (elbow flexion)[i]	Supervised Unsupervised	0.12 0.08	NA	NA	NA
Quality of life	Supervised Unsupervised	0.22 0.16	0.03 NA	NA	0.27
Self-reported physical functioning	Supervised Unsupervised	0.13 0.23	0.00 NA	NA	0.16
Maintenance–setting level					
Physical therapy network	(i) Existence of a broad network of PTs trained to guide patients with cancer with exercise during and after chemotherapy (ii) All PTs within the network follow mandatory refresher courses and have to pass summative tests related to these courses (iii) The network covers most of the populated areas in the Netherlands, and an specialized PT is available within a 15 min commute for most people				
Oncology specializations for physical therapists	2 types of specializations: (1) Around 127 physical therapists have a master degree in oncology physical therapy, a three-year (60–96ECs) part-time study which covers both hands-on treatment of oncology patients and guidance of patients in exercise programs (2) Over 550 PTs working at over 700 locations in the Netherlands have been specifically educated on exercise treatment during and after treatment, via the Onconet courses executed by the Dutch Institute of Allied Healthcare. These PTs have received 67 hours or more of additional training in subjects such as basic oncology, exercise oncology, behavioral support, dealing with cancer-specific side effects, dealing with comorbidities, using clinimetrics, and clinical reasoning in an oncology context				

*Indicate effects in favor of the control group. *EC*: European credits; *HI*: high intensity; *IQR*: interquartile range; *LMI*: low-to-moderate intensity; *MHI*: moderate-to-high intensity; *PT*: physical therapist; *QALY*: quality-adjusted life year; *WLC*: wait list control. [a]Unpublished results of the REACT trial (additional analysis on data from patients with breast cancer only); analysis on predictors for participation with multivariable logistic regression; analysis on predictors for adherence performed with univariate logistic regression; [b]relatively high participation rate of 52% due to the trials within cohorts (TwiCs) design; [c]a comparison of characteristics between participants and a subgroup of nonparticipants (patients who did not want to exercise) [26]; [d]a comparison of characteristics between participants and a subgroup of nonparticipants (who want to exercise by themselves); [e]combined characteristics of 2 separate studies as reported in Gal et al., 2021 [32] combined with unpublished results REACT[a]; [f]in case, effect sizes of 2 studies were available for the same outcome, and this is reported for instance as 0.23 and 0.29; [g]evaluated using cardiopulmonary exercise testing (peak power output, watt) [18, 27] and steep ramp test (maximal short exercise capacity, watt) [24]; [h]evaluated using a cybex dynamometer at angular velocities of 60°/s; [i]evaluated with a handheld dynamometer; [j]unpublished results of the PACT trial; [k]unpublished results of the UMBRELLA Fit trial; [l]the percentages presented are calculated by the number of specific suggestions divided by the total number of suggestions; [m]the percentages are calculated by the number of specific suggestions divided by the number of PTs that rated their satisfaction ($n = 20$); [n]attendance: number of supervised exercise sessions attended/number of supervised sessions offered; [o]compliance: achieved intensity and volume/prescribed intensity and volume of both resistance and endurance exercises; [p]predictors are reported if $p \leq 0.05$; [q]performing the total prescribed number of minutes; [r]performing the prescribed number of minutes at or above the VT.

in the Dutch trials suggested that they would appreciate being able to reschedule missed exercise sessions, add more variety to the prescribed exercises, and combine the exercise sessions with yoga [22]. This was also found in a study of women with ovarian cancer [65]. Taking patient preferences into account can increase enjoyment, which, in turn, can have a beneficial effect on exercise maintenance [66]. At the same time, to achieve their goals and the desired health benefits, it is important that patients are informed on the exercise frequency, intensity, type, and time (FITT) required. Patient satisfaction, and thereby potentially exercise maintenance, can be further improved by taking sufficient time for exercise familiarisation, optimizing exercise scheduling in relation to chemotherapy administrations [67], and adequate tailoring of exercise intensity to the individual's fitness level.

The generally lower level of satisfaction reported for the home-based exercise counselling compared to supervised exercise may be related to the limited time devoted by healthcare professionals (e.g., physical therapists or nurse practitioners) (HCPs) to instructing and motivating patients and to individualizing the home-based exercises. Motivational interviewing appeared to be an effective technique to improve exercise behavior of patients with cancer in some studies [68, 69], but not all [70]. Dedicated time, and better training in exercise counselling, and development of supportive tools may improve the counselling skills of HCPs delivering exercise programs.

3.3. Adoption

3.3.1. Summary of Results of Dutch RCTs. Most patients in the Dutch RCTs were recruited from both community and university hospitals and were referred to a physical therapist specifically trained to work with patients with cancer, located close to the patients' homes. The physical therapists who delivered the intervention after completion of cancer treatment were generally satisfied with the content of the trial intervention (supervised aerobic and resistance exercise two days per week, supplemented by counseling on unsupervised exercise for three other days). The average satisfaction score was 7.5 (on a 1–10 scale, Table 3). While, overall, the physical therapists were satisfied with the exercise intervention, some reported that they would have preferred to prescribe more variation in the resistance exercises (20%) that the exercise counseling was too time-consuming (20%) and that physical therapists could benefit from some additional training in this regard (10%) (Table 3).

3.3.2. Reflections and Opportunities to Improve Adoption. Few studies have described experiences of professionals delivering exercise interventions to patients with cancer treated with curative intent in the context of a trial. More variation in exercises has also been suggested by other studies, in order to prevent boredom, better tailor exercises to patients' preferences, needs (e.g., functional training), or capabilities, and to add exercise types other than resistance or aerobic exercises, such as balance exercises [65, 71]. In addition, physical therapists and personal trainers have reported that guidance of a group of patients can be challenging (e.g., dealing with different types of group dynamics; providing sufficient attention to individual patients' abilities and needs) [72, 73]. This indicates the importance of qualified trainers and preferably small group sizes although the latter needs to be balanced with affordability.

Results of focus groups in various HCPs working in primary or secondary care in the Netherlands (e.g., physicians, nurses, and physical therapists) reported that insufficient evidence about benefits of exercise programs was a barrier for their use [71]. This can be a reason for not referring patients to exercise programs. Hence, efforts to disseminate the evidence on the effects of exercise on cancer outcomes will likely accelerate the implementation of exercise as part of standard cancer care [74]. Additionally, these exercise programs should be adequately tailored to the individual patients' needs, capabilities, and preferences [71] while taking evidence-based exercise frequency, intensity, type, and time (FITT) into account.

3.4. Implementation.

Implementation was evaluated based on (a) exercise adherence and (b) resources and intervention costs [75].

3.4.1. Exercise Adherence

(1) Summary of Results of Dutch RCTs. The median attendance rates of supervised exercise in the Dutch trials varied between 77% and 98% and were 71% for unsupervised exercise (Table 3). Median compliance rates ranged between 81% and 88% for moderate intensity aerobic exercises, between 50% and 87% for HI aerobic exercises, and between 84% and 94% for resistance exercises (Table 3). The most frequently reported reasons for not attending the sessions during chemotherapy were feeling too ill (53%) and logistical reasons (30%). During chemotherapy, higher disease stage, having a partner, higher educational level, and a lower body mass index (BMI) were significantly associated with better attendance [20, 22]. Results on predictors of compliance to the prescribed exercises during and after treatment suggested a difference between exercise type (resistance versus aerobic), intensity (LMI versus HI), and delivery mode (supervised versus unsupervised) [20]. In general, after cancer treatment, psychosocial factors, such as higher self-efficacy and having a more positive attitude towards exercise, were associated with a higher attendance and compliance to HI but not to LMI exercise (Table 3).

(2) Reflections and Opportunities to Improve Implementation. The exercise adherence rates and the diversity in predictors of adherence in Dutch studies are in line with previous findings from other studies [76–78]. This diversity can be explained by differences in exercise prescriptions between studies and in the predictors studied. The finding that treatment-related adverse effects ("feeling too ill") accounted for over half of the total missed sessions is also in line with other exercise studies in patients with breast cancer

receiving chemotherapy [79, 80]. Consideration of side effects as part of exercise program design has been proposed, for example, by using "chemotherapy-periodized" exercise prescriptions that take chemotherapy side effects into account [67]. The finding that patients with lower exercise self-efficacy and more negative attitudes towards exercise had more difficulties with adhering to HI exercise suggests that realistic goal setting and starting at a lower intensity, to gain confidence before progressing to HI exercise, may be useful to improve adherence of these patients.

Previous systematic literature reviews found exercise history to be associated with better exercise adherence [77, 78]. This was not supported by the results from the Dutch trials, which suggests that other factors may be more important. It should be noted that the overall adherence reported in the Dutch trials was relatively high. This may not, however, turn out to be the case in clinical practice, due to variation in motivation and less emphasis on required adherence [73, 81]. Future studies in daily clinical practice that yield real-world data on exercise adherence, collected via electronic medical records, might help elucidate which factors are associated significantly with adherence to exercise outside the trial context and to identify subgroups of patients and cancer survivors that might require adjustments to the exercise intervention or psychosocial and behavioral support for improving adherence.

3.4.2. Resources and Intervention Costs

(1) Summary of Results of Dutch RCTs. Two of the Dutch trials assessed the cost-effectiveness of the exercise interventions during treatment. In one trial, the supervised exercise intervention during chemotherapy was found to be cost-effective with a probability of 45% at a willingness-to-pay of 20.000€/quality-adjusted life year (QALY) [25]. The other trial reported that, at a willingness-to-pay of 20.000€/QALY, the probability that the intervention would be cost-effective was very low (2%) [21]. The unsupervised exercise intervention was not cost-effective (25% probability for cost-effectiveness at a willingness-to-pay of 20.000€/QALY). After completion of chemotherapy, a HI-exercise program was more cost-effective than a LMI exercise program [29], with a probability of 91% at a willingness-to-pay of 20.000€/QALY.

(2) Reflections and Opportunities for Further Implementation. Results on the cost-effectiveness of exercise interventions in Dutch trials were mixed, possibly explained by contamination or differences in follow-up time [21, 25]. Previous systematic reviews showed that supervised exercise interventions and multimodal interventions were cost-effective when they yielded significant beneficial effects on health outcomes such as energy, fear of recurrence, mood, and pain [82, 83].

In the Netherlands, exercise supervision from a physical therapist is currently not reimbursed by basic healthcare insurance. However, exercise sessions for patients who have had surgery prior to their chemotherapy or received radiotherapy treatment in the past 6 months can be reimbursed from the 21st session onwards until 1 to 2 years (depending on the treatment and insurance). Additionally, biweekly one-hour supervised exercise sessions can only be provided in group sessions of 2–10 persons because physical therapists are allowed to invoice for a maximum of 30 minutes per day per person. Fortunately, group sessions are often appreciated by cancer survivors and facilitate peer support [22, 62, 65] and may consequently improve adherence rates. On the other hand, group sessions are often less flexible with regard to exercise times, which has been reported as barrier to (adhering to) exercise programs [22]. Also, group sessions are not suitable for every patient as some patients feel uncomfortable with group exercise and/or may require more intensive coaching than possible in group settings.

More information on the cost-effectiveness of exercise interventions and consideration of other healthcare reimbursement strategies (e.g., bundled-payment models) could be helpful to better inform discussions among health policy-makers and insurers about appropriate reimbursement policy and insurance coverage for exercise interventions during and after chemotherapy. Future cost-effectiveness evaluations need to take into account that higher chemotherapy completion rates resulting from exercise interventions may result in higher costs of medication and secondary healthcare but also higher survival rates [84] and that work absenteeism may be underestimated when absence, beyond the percentage sick leave that is agreed upon by patients and employers, is not reported as absenteeism days [25].

3.5. Maintenance. In this section, we evaluated maintenance at the *patient level*, describing long-term effects of the intervention, and at the *organizational level*, describing the extent to which the exercise programs have been institutionalized and integrated into routine practice, as well as the policies enabling program sustainability.

3.5.1. Patient Level

(1) Summary of Results of Dutch RCTs. Exercise *during* chemotherapy did not yield significant effects on aerobic fitness, self-reported fatigue, or HRQoL at follow-up (i.e., 6, 8, and 48 months) [19, 23]. However, patients who participated in an exercise program *after* completing their oncological treatment successfully maintained their improved levels of cardiorespiratory fitness and HRQoL at one-year postintervention (Table 3). The positive intervention effects on HRQoL observed at one-year follow-up were significantly larger for HI compared to LMI exercise (Table 3).

(2) Reflections and Opportunities for Improving Maintenance at the Patient Level. The limited maintenance of intervention effects on most outcomes might be explained by the uptake of exercise by control group participants after the completion of chemotherapy or the specific focus on improving outcomes during the intervention period without sufficient

incorporation of behavioral change techniques to maintain healthy behaviors in the long term.

Sustained benefits on aerobic fitness were found one year after completion of exercise interventions and after cancer treatment. Nevertheless, peakVO_2 levels were still "poor," as compared to healthy adults [29]. This might indicate that a 12-week program might be too short for patients to fully return to normative values, and patients may not have received sufficient guidance to continue exercising at home at sufficient intensities after completion of the trial to continue improving their peakVO_2. This is in line with the previously mentioned feedback of physical therapists that they had insufficient time for counseling and expressed a need for additional education (Table 3). Further development of tools to improve the quality of counseling and efficient integration into daily practice might improve maintenance of adequate exercise levels to further improve peakVO_2. This could be achieved by improved incorporation of behavioral change techniques, such as "instruction on how to perform the behavior," "feedback and self-monitoring of behavior," and "goal-setting (behavior)" [43]. Education on how to use behavior change techniques may help to overcome some perceived barriers of exercise maintenance that have been reported by patients with breast cancer, including *psychological barriers* (e.g., lack of motivation, fears, dislike of gym, or not being the "sporty type"), *physical barriers* (e.g., ageing, side effects of cancer treatment, and other comorbidities, weight gain), and *contextual* and *environmental barriers* (related to employment, traditional female care-giving roles, access to facilities, and seasonal weather) [85].

3.5.2. Organizational Level

(1) Summary of Results of Dutch RCTs. For the conduct of the Dutch trials, physical therapists were trained to supervise patients with cancer in exercising during chemotherapy and after treatment, within the initiated Onconet network. After trial completion, the Onconet foundation further educated physical therapists on the content and delivery of exercise programs for patients with cancer, and thereby consolidated and expanded a physical therapist network. The education also includes mandatory refresher courses where physical therapists are updated on results from recent studies. Currently, the network of physical therapists specialized in guiding patients with cancer is nationwide, with over 700 locations mostly within a 15-minute travel distance from any address. Additionally, MSc-level programs are available to educate physical therapists in oncology.

(2) Reflections and Opportunities for Improving Maintenance at the Organizational Level. In the Netherlands, currently, most supervised exercise interventions are offered by allied healthcare professionals. In primary care, this is primarily via physical therapists working in private clinics. Exercise can also be offered as part of a multidisciplinary rehabilitation program in secondary (hospitals) or tertiary (rehabilitation clinics) care. Outside of the healthcare system, fitness trainers with oncology specialization are increasingly available. These fitness professionals mainly deliver exercise interventions to patients who have completed treatment at least 3 months earlier [71].

Results from a qualitative study in the Netherlands indicate that HCPs working in primary care (e.g., general practitioners, physical therapists) perceive collaboration, communication, and referral between primary and secondary HCPs to be suboptimal [71], whereas HCPs working in secondary care (e.g., physicians, nurses, and paramedics) raised general concerns about inadequate cooperation and networks between healthcare institutes [71]. The HCPs suggested that more use of health information technology, improved access to electronic health records, improved rehabilitation guidelines with recommendations about roles and responsibilities of each HCP, and better networks would improve the implementation of exercise in cancer care [71].

Internationally, the most reported barriers to integrating exercise in oncology settings are at the organizational level [86]. These barriers are related to the limited capacity and resources of staff, including insufficient time to prescribe and refer patients to exercise programs, and to the organization of care processes (e.g., absence of an established care pathway or structure) [86]. To reduce organizational barriers in the Netherlands, the "Taskforce Cancer Survivorship Care" has been established since 2017. In this taskforce, HCPs, policymakers, researchers, and patient organizations join forces aiming to improve attention for and optimization of quality of care over the whole cancer continuum and to improve organizational structures by better coordination between HCPs [87]. The taskforce also pursues an increase of physical therapist participation in multidisciplinary and oncology care networks, enabling further knowledge exchange and improved communication with other HCPs.

4. Discussion

In this study, we have used the RE-AIM framework to describe the potential for implementation of exercise interventions for patients with breast cancer, based on four RCTs previously conducted in the Netherlands. Results from these RCTs demonstrated that exercise during and after treatment has beneficial effects on aerobic fitness, fatigue, and HRQoL in patients with breast cancer. Additionally, both patients and physical therapists were generally satisfied with the intervention, but there were challenges to exercise maintenance.

The current network of physical therapists specialized in oncology that was initiated at the start of the trials continues to expand and represents a fruitful interaction between research and clinical practice. The current evaluation revealed key opportunities to further optimize implementation of exercise programs in the oncology setting. First, there is room to further increase knowledge and awareness among HCPs of the potential benefits of exercise and to improve organizational structures to increase referral to supervised programs. Improving awareness and referral requires more insight into perspectives of organizational

stakeholders and policymakers and optimal dissemination of patient information between HCPs for which a whole system approach is needed [71, 86].

Second, although the interventions in the Dutch exercise trials were tailored to individuals' fitness level and treatment side effects, specific subgroups of patients, such as the elderly and those who are in poor physical condition, are more prone to nonparticipation and appear not to benefit as much [1, 56]. These patients may benefit from an even more personalized and goal-directed functional exercise training program. Such programs have been shown to be feasible and promising in patients with metastatic breast cancer [88]. Similarly, a patient-centred, goal-directed, self-management enhancing functional exercise program that is based on a biopsychosocial model, Coach2move, has shown to be (cost-)effective in improving physical activity and function in community dwelling older adults with mobility problems [89]. A personalized program that is tailored to the individual's needs and preferences, including behavioral change techniques such as "goal-setting" and "feedback and self-monitoring of behavior," may also facilitate sustained benefits over time. Successful inclusion of behavioral change techniques as part of exercise supervision may require additional schooling for physical therapists.

Finally, the implementation of exercise programs for all patients with cancer is currently hampered by the lack of reimbursement of physical therapist-guided exercise programs during and after treatment. The Taskforce Cancer Survivorship aims to improve healthcare during and after cancer treatment, and one of the pillars of the Taskforce is to improve reimbursement of allied healthcare [87].

Some limitations of our study should be noted. Because it has been suggested that implementation strategies must be tailored to its context to improve effectiveness [90], we summarized exercise trials with a homogeneity in settings, circumstances, and conditions, thereby specifically focusing on patients with breast cancer in the Netherlands. Hence, caution is needed when generalizing our findings to other countries with different healthcare systems and to patients with other cancer types or advanced cancer [91, 92]. On the other hand, the findings from Dutch trials seem to echo those of studies conducted in other countries. Additionally, we based our assessments on a retrospective evaluation of the potential impact of exercise intervention trials. Our findings might have been different if data from the clinical practice setting had been collected prospectively (e.g., information on treatment referral and treatment fidelity outside of the context of a trial). Future studies should, therefore, prospectively evaluate the implementation of exercise interventions using the RE-AIM framework, for example, by collecting real-world data to describe characteristics of patients who are referred to exercise interventions and to register the delivered exercise prescription in terms of FITT-factors and the resulting changes in aerobic fitness, physical functioning, HRQoL, and achievement of physical therapy goals. This would also facilitate obtaining information about and from patients with comorbidities or those who otherwise would be excluded from trials or referred to less extent to trials [93, 94]. Such collection of real-world data would be facilitated by an adequate registration system to structurally monitor clinical practice, in order to learn from every patient, and subsequently optimize healthcare [95]. Moreover, future research could benefit from hybrid designs, in which elements of clinical effectiveness and implementation research are combined [73, 96]. This might speed up the translation of research's finding into clinical practice 97.

5. Conclusion

The RE-AIM framework facilitated a retrospective evaluation of the impact of exercise interventions and their potential for implementation in clinical practice. We found acceptable RE-AIM outcomes in terms of participation rates, intervention effects, satisfaction of patients and physical therapists, and adherences rates within the trial context. Additionally, an established network of physical therapists educated in oncology facilitates the maintenance of exercise interventions outside of clinical trials. We have recommended several steps that could be taken to further improve implementation of exercise programs for cancer patients and survivors, including improved referral (*reach*), improved tailoring of exercise interventions to individual needs and preferences, improved attention to maintenance of exercise behavior (*effectiveness, adoption, implementation, and maintenance*), and improved reimbursement (*reach and maintenance*).

Data Availability

Data presented in this trial are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors contributed to the study conception and design. Marieke R. Ten Tusscher, Laurien M. Buffart, Caroline S. Kampshoff, Hanna Van Waart, and Roxanne Gal collected the aggregate data. Marieke R. Ten Tusscher and Laurien M. Buffart performed additional subgroup analysis. Marieke R. Ten Tusscher and Laurien M. Buffart wrote the first draft of the manuscript. Martijn M. Stuiver, Caroline S. Kampshoff, Rosalie J. Huijsmans, Neil K. Aaronson, Miranda Velthuis, Roxanne Gal, Hanna Van Waart, and Anne M. May commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

[1] M. G. Sweegers, T. M. Altenburg, J. Brug et al., "Effects and moderators of exercise on muscle strength, muscle function and aerobic fitness in patients with cancer: a meta-analysis of individual patient data," *British Journal of Sports Medicine*, vol. 53, no. 13, p. 812, 2019.

[2] J. K. van Vulpen, M. G. Sweegers, P. H. M. Peeters et al., "Moderators of exercise effects on cancer-related fatigue:

a meta-analysis of individual patient data," *Medicine & Science in Sports & Exercise*, vol. 52, no. 2, pp. 303–314, 2020.

[3] L. M. Buffart, J. Kalter, M. G. Sweegers 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 Treatment Reviews*, vol. 52, pp. 91–104, 2017.

[4] K. L. Campbell, K. M. Winters-Stone, J. Wiskemann et al., "Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable," *Medicine & Science in Sports & Exercise*, vol. 51, no. 11, pp. 2375–2390, 2019.

[5] World Cancer Research Fund/American Institute for Cancer Research, *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective*, AICR, Washingon DC, USA, 2007.

[6] A. Campbell, C. Stevinson, and H. Crank, "The BASES expert statement on exercise and cancer survivorship," *Journal of Sports Sciences*, vol. 30, no. 9, pp. 949–952, 2012.

[7] R. Segal, C. Zwaal, E. Green, J. R. Tomasone, A. Loblaw, and T. Petrella, "Exercise for people with cancer: a clinical practice guideline," *Current Oncology*, vol. 24, no. 1, pp. 40–46, 2017.

[8] C. L. Rock, C. Thomson, T. Gansler et al., "American Cancer Society guideline for diet and physical activity for cancer prevention," *CA: A Cancer Journal for Clinicians*, vol. 70, no. 4, pp. 245–271, 2020.

[9] S. C. Hayes, R. U. Newton, R. R. Spence, and D. A. Galvão, "The Exercise and Sports Science Australia position statement: exercise medicine in cancer management," *Journal of Science and Medicine in Sport*, vol. 22, no. 11, pp. 1175–1199, 2019.

[10] J. A. Ligibel, K. Bohlke, A. M. May et al., "Exercise, diet, and weight management during cancer treatment: ASCO guideline," *Journal of Clinical Oncology*, vol. 40, no. 22, pp. 2491–2507, 2022.

[11] K. L. Campbell, P. Cormie, S. Weller et al., "Exercise recommendation for people with bone metastases: expert consensus for health care providers and exercise professionals," *JCO Oncology Practice*, vol. 18, no. 5, pp. e697–e709, 2022.

[12] M. G. Sweegers, M. C. M. Doormaal van, D. Conijn, and M. M. Stuiver, "KNGF-richtlijn Oncologie," 2022, https://www.kngf.nl/kennisplatform/richtlijnen/oncologie.

[13] S. M. White, E. McAuley, P. A. Estabrooks, and K. S. Courneya, "Translating physical activity interventions for breast cancer survivors into practice: an evaluation of randomized controlled trials," *Annals of Behavioral Medicine*, vol. 37, no. 1, pp. 10–19, 2009.

[14] R. E. Glasgow, T. M. Vogt, and S. M. Boles, "Evaluating the public health impact of health promotion interventions: the RE-AIM framework," *American Journal of Public Health*, vol. 89, no. 9, pp. 1322–1327, 1999.

[15] R. S. Kessler, E. P. Purcell, R. E. Glasgow, L. M. Klesges, R. M. Benkeser, and C. J. Peek, "What does it mean to "employ" the RE-AIM model?" *Evaluation & the Health Professions*, vol. 36, no. 1, pp. 44–66, 2013.

[16] J. K. van Vulpen, P. H. Peeters, M. J. Velthuis, E. van der Wall, and A. M. May, "Effects of physical exercise during adjuvant breast cancer treatment on physical and psychosocial dimensions of cancer-related fatigue: a meta-analysis," *Maturitas*, vol. 85, pp. 104–111, 2016.

[17] N. Travier, M. J. Velthuis, C. N. Steins Bisschop et al., "Effects of an 18-week exercise programme started early during breast cancer treatment: a randomised controlled trial," *BMC Medicine*, vol. 13, no. 1, p. 121, 2015.

[18] M. J. Velthuis, A. M. May, R. A. Koppejan-Rensenbrink et al., "Physical activity during cancer treatment (PACT) study: design of a randomised clinical trial," *BMC Cancer*, vol. 10, no. 1, p. 272, 2010.

[19] L. Witlox, A. E. Hiensch, M. J. Velthuis et al., "Four-year effects of exercise on fatigue and physical activity in patients with cancer," *BMC Medicine*, vol. 16, no. 1, p. 86, 2018.

[20] L. Witlox, M. J. Velthuis, J. H. Boer et al., "Attendance and compliance with an exercise program during localized breast cancer treatment in a randomized controlled trial: the PACT study," *PLoS One*, vol. 14, no. 5, Article ID e0215517, 2019.

[21] A. M. May, M. J. Bosch, M. J. Velthuis et al., "Cost-effectiveness analysis of an 18-week exercise programme for patients with breast and colon cancer undergoing adjuvant chemotherapy: the randomised PACT study," *BMJ Open*, vol. 7, no. 3, Article ID e012187, 2017.

[22] H. van Waart, L. M. Buffart, M. M. Stuiver, W. H. van Harten, G. S. Sonke, and N. K. Aaronson, "Adherence to and satisfaction with low-intensity physical activity and supervised moderate-high intensity exercise during chemotherapy for breast cancer," *Supportive Care in Cancer*, vol. 28, no. 5, pp. 2115–2126, 2020.

[23] H. van Waart, M. M. Stuiver, W. H. van Harten et al., "Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial," *Journal of Clinical Oncology*, vol. 33, no. 17, pp. 1918–1927, 2015.

[24] H. van Waart, M. M. Stuiver, W. H. van Harten, G. S. Sonke, and N. K. Aaronson, "Design of the Physical exercise during Adjuvant Chemotherapy Effectiveness Study (PACES): a randomized controlled trial to evaluate effectiveness and cost-effectiveness of physical exercise in improving physical fitness and reducing fatigue," *BMC Cancer*, vol. 10, no. 1, p. 673, 2010.

[25] H. van Waart, J. M. van Dongen, W. H. van Harten et al., "Cost-utility and cost-effectiveness of physical exercise during adjuvant chemotherapy," *The European Journal of Health Economics*, vol. 19, no. 6, pp. 893–904, 2017.

[26] H. van Waart, W. H. van Harten, L. M. Buffart, G. S. Sonke, M. M. Stuiver, and N. K. Aaronson, "Why do patients choose (not) to participate in an exercise trial during adjuvant chemotherapy for breast cancer?" *Psycho-Oncology*, vol. 25, no. 8, pp. 964–970, 2016.

[27] C. S. Kampshoff, L. M. Buffart, G. Schep, W. van Mechelen, J. Brug, and M. J. Chinapaw, "Design of the Resistance and Endurance exercise after ChemoTherapy (REACT) study: a randomized controlled trial to evaluate the effectiveness and cost-effectiveness of exercise interventions after chemotherapy on physical fitness and fatigue," *BMC Cancer*, vol. 10, no. 1, p. 658, 2010.

[28] C. S. Kampshoff, M. J. Chinapaw, J. Brug et al., "Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: results of the Resistance and Endurance exercise after ChemoTherapy (REACT) study," *BMC Medicine*, vol. 13, no. 1, p. 275, 2015.

[29] C. S. Kampshoff, J. M. van Dongen, W. van Mechelen et al., "Long-term effectiveness and cost-effectiveness of high versus low-to-moderate intensity resistance and endurance exercise interventions among cancer survivors," *J Cancer Surviv*, vol. 12, no. 3, pp. 417–429, 2018.

[30] C. S. Kampshoff, W. van Mechelen, G. Schep et al., "Participation in and adherence to physical exercise after

completion of primary cancer treatment," *International Journal of Behavioral Nutrition and Physical Activity*, vol. 13, no. 1, p. 100, 2016.

[31] R. Gal, E. M. Monninkhof, R. H. H. Groenwold et al., "The effects of exercise on the quality of life of patients with breast cancer (the UMBRELLA Fit study): study protocol for a randomized controlled trial," *Trials*, vol. 18, no. 1, p. 504, 2017.

[32] R. Gal, E. M. Monninkhof, C. H. van Gils et al., "Effects of exercise in breast cancer patients: implications of the trials within cohorts (TwiCs) design in the UMBRELLA Fit trial," *Breast Cancer Research and Treatment*, vol. 190, no. 1, pp. 89–101, 2021.

[33] J. C. Moullin, K. S. Dickson, N. A. Stadnick et al., "Ten recommendations for using implementation frameworks in research and practice," *Implementation Science Communications*, vol. 1, no. 1, p. 42, 2020.

[34] J. Cohen, *Statistical Power Analysis for the Behavioral Sciences*, Academic Press, Cambridge, MA, USA, 4th edition, 2013.

[35] J. C. Hoover, A. M. Alenazi, M. M. Alshehri et al., "Recruiting and retaining patients with breast cancer in exercise trials: a meta-analysis," *Translational Journal of the American College of Sports Medicine*, vol. 6, no. 1, Article ID e000149, 2021.

[36] R. Gal, E. M. Monninkhof, C. H. van Gils et al., "The Trials within Cohorts design faced methodological advantages and disadvantages in the exercise oncology setting," *Journal of Clinical Epidemiology*, vol. 113, pp. 137–146, 2019.

[37] H. Wittink and J. Oosterhaven, "Patient education and health literacy," *Musculoskeletal Science and Practice*, vol. 38, pp. 120–127, 2018.

[38] G. Kreps and L. Neuhauser, "Designing health information programs to promote the health and well-being of vulnerable populations: the benefits of evidence-based strategic health communication," *Meeting Health Information Needs Outside of Healthcare: Opportunities and Challenges*, vol. 12, pp. 3–17, 2015.

[39] S. M. Gollhofer, J. Wiskemann, M. E. Schmidt et al., "Factors influencing participation in a randomized controlled resistance exercise intervention study in breast cancer patients during radiotherapy," *BMC Cancer*, vol. 15, no. 1, p. 186, 2015.

[40] S. J. Hardcastle, C. Maxwell-Smith, S. Kamarova, S. Lamb, L. Millar, and P. A. Cohen, "Factors influencing non-participation in an exercise program and attitudes towards physical activity amongst cancer survivors," *Supportive Care in Cancer*, vol. 26, no. 4, pp. 1289–1295, 2018.

[41] B. K. Clifford, D. Mizrahi, C. X. Sandler et al., "Barriers and facilitators of exercise experienced by cancer survivors: a mixed methods systematic review," *Supportive Care in Cancer*, vol. 26, no. 3, pp. 685–700, 2018.

[42] S. Michie, M. Richardson, M. Johnston et al., "The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions," *Annals of Behavioral Medicine*, vol. 46, no. 1, pp. 81–95, 2013.

[43] V. Hailey, A. Rojas-Garcia, and A. P. Kassianos, "A systematic review of behaviour change techniques used in interventions to increase physical activity among breast cancer survivors," *Breast Cancer*, vol. 29, no. 2, pp. 193–208, 2022.

[44] Zorgpad Professional, "Bewegen bij kanker (ziekenhuis)," 2023, https://zorgpadprofessional.noordhoff.nl/leerpad/bewegen-bij-kanker-ziekenhuis/.

[45] S. M. Bluethmann, K. Basen-Engquist, S. W. Vernon et al., "Grasping the 'teachable moment': time since diagnosis, symptom burden and health behaviors in breast, colorectal and prostate cancer survivors," *Psycho-Oncology*, vol. 24, no. 10, pp. 1250–1257, 2015.

[46] K. M. Sturgeon, C. Fisher, G. McShea, S. K. Sullivan, D. Sataloff, and K. H. Schmitz, "Patient preference and timing for exercise in breast cancer care," *Supportive Care in Cancer*, vol. 26, no. 2, pp. 507–514, 2018.

[47] K. H. Schmitz, A. M. Campbell, M. M. Stuiver et al., "Exercise is medicine in oncology: engaging clinicians to help patients move through cancer," *CA: A Cancer Journal for Clinicians*, vol. 69, no. 6, pp. 468–484, 2019.

[48] L. W. Jones, K. S. Courneya, A. S. Fairey, and J. R. Mackey, "Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: a single-blind, randomized controlled trial," *Annals of Behavioral Medicine*, vol. 28, no. 2, pp. 105–113, 2004.

[49] K. A. Nyrop, A. M. Deal, G. R. Williams, E. J. Guerard, M. Pergolotti, and H. B. Muss, "Physical activity communication between oncology providers and patients with early-stage breast, colon, or prostate cancer," *Cancer*, vol. 122, no. 3, pp. 470–476, 2016 Feb 1.

[50] J. A. Ligibel, L. W. Jones, A. M. Brewster et al., "Oncologists' attitudes and practice of addressing diet, physical activity, and weight management with patients with cancer: findings of an ASCO survey of the oncology workforce," *Journal of Oncology Practice*, vol. 15, no. 6, pp. e520–e528, 2019.

[51] H. Arem, X. Duan, D. K. Ehlers, M. E. Lyon, J. H. Rowland, and S. K. Mama, "Provider discussion about lifestyle by cancer history: a nationally representative survey," *Cancer Epidemiology, Biomarkers & Prevention*, vol. 30, no. 2, pp. 278–285, 2021.

[52] J. Nauta, F. van Nassau, A. J. Bouma et al., "Facilitators and barriers for the implementation of exercise are medicine in routine clinical care in Dutch university medical centres: a mixed methodology study on clinicians' perceptions," *BMJ Open*, vol. 12, no. 3, Article ID e052920, 2022.

[53] M. Nadler, D. Bainbridge, J. Tomasone, O. Cheifetz, R. A. Juergens, and J. Sussman, "Oncology care provider perspectives on exercise promotion in people with cancer: an examination of knowledge, practices, barriers, and facilitators," *Supportive Care in Cancer*, vol. 25, no. 7, pp. 2297–2304, 2017.

[54] F. A. Albert, A. E. O. Malau-Aduli, M. J. Crowe, and B. S. Malau-Aduli, "Optimising care coordination strategies for physical activity referral scheme patients by Australian health professionals," *PLoS One*, vol. 17, no. 7, Article ID e0270408, 2022.

[55] M. van der Leeden, R. J. Huijsmans, E. Geleijn et al., "Tailoring exercise interventions to comorbidities and treatment-induced adverse effects in patients with early stage breast cancer undergoing chemotherapy: a framework to support clinical decisions," *Disability & Rehabilitation*, vol. 40, no. 4, pp. 486–496, 2018.

[56] L. M. Buffart, M. G. Sweegers, A. M. May et al., "Targeting exercise interventions to patients with cancer in need: an individual patient data meta-analysis," *Journal of the National Cancer Institute: Journal of the National Cancer Institute*, vol. 110, no. 11, pp. 1190–1200, 2018.

[57] J. M. Scott, E. C. Zabor, E. Schwitzer et al., "Efficacy of exercise therapy on cardiorespiratory fitness in patients with cancer: a systematic review and meta-analysis," *Journal of Clinical Oncology*, vol. 36, no. 22, pp. 2297–2305, 2018.

[58] D. H. Paterson, D. A. Cunningham, J. J. Koval, and C. M. St Croix, "Aerobic fitness in a population of independently living men and women aged 55-86 years," *Medicine & Science in Sports & Exercise*, vol. 31, no. 12, pp. 1813–1820, 1999.

[59] S. Mijwel, A. Jervaeus, K. A. Bolam et al., "High-intensity exercise during chemotherapy induces beneficial effects 12 months into breast cancer survivorship," *J Cancer Surviv*, vol. 13, no. 2, pp. 244–256, 2019.

[60] K. Tsuji, Y. J. Matsuoka, and E. Ochi, "High-intensity interval training in breast cancer survivors: a systematic review," *BMC Cancer*, vol. 21, no. 1, p. 184, 2021.

[61] P. Lopez, D. R. Taaffe, R. U. Newton, L. M. Buffart, and D. A. Galvão, "What is the minimal dose for resistance exercise effectiveness in prostate cancer patients? Systematic review and meta-analysis on patient-reported outcomes," *Prostate Cancer and Prostatic Diseases*, vol. 24, no. 2, pp. 465–481, 2021.

[62] C. Emslie, F. Whyte, A. Campbell et al., "I wouldn't have been interested in just sitting round a table talking about cancer'; exploring the experiences of women with breast cancer in a group exercise trial," *Health Education Research*, vol. 22, no. 6, pp. 827–838, 2006.

[63] M. L. Luoma, L. Hakamies-Blomqvist, C. Blomqvist, R. Nikander, M. Gustavsson-Lilius, and T. Saarto, "Experiences of breast cancer survivors participating in a tailored exercise intervention-a qualitative study," *Anticancer Research*, vol. 34, no. 3, pp. 1193–1199, 2014.

[64] M. Browall, S. Mijwel, H. Rundqvist, and Y. Wengstrom, "Physical activity during and after adjuvant treatment for breast cancer: an integrative review of women's experiences," *Integrative Cancer Therapies*, vol. 17, no. 1, pp. 16–30, 2018.

[65] S. Stelten, L. R. C. W. van Lonkhuijzen, Y. A. W. Hartman et al., "Experiences, adherence and satisfaction with a combined exercise and dietary intervention for patients with ovarian cancer undergoing chemotherapy: a mixed-methods study," *Gynecologic Oncology*, vol. 165, no. 3, pp. 619–628, 2022 2022.

[66] D. S. Teixeira, F. Rodrigues, L. Cid, and D. Monteiro, "Enjoyment as a predictor of exercise habit, intention to continue exercising, and exercise frequency: the intensity traits discrepancy moderation role," *Frontiers in Psychology*, vol. 13, Article ID 780059, 2022.

[67] A. A. Kirkham, K. A. Bland, D. S. Zucker et al., "Chemotherapy-periodized" exercise to accommodate for cyclical variation in fatigue," *Medicine & Science in Sports & Exercise*, vol. 52, no. 2, pp. 278–286, 2020.

[68] J. C. Spencer and S. B. Wheeler, "A systematic review of Motivational Interviewing interventions in cancer patients and survivors," *Patient Education and Counseling*, vol. 99, no. 7, pp. 1099–1105, 2016.

[69] J. A. Bennett, K. S. Lyons, K. Winters-Stone, L. M. Nail, and J. Scherer, "Motivational interviewing to increase physical activity in long-term cancer survivors: a randomized controlled trial," *Nursing Research*, vol. 56, no. 1, pp. 18–27, 2007.

[70] A. M. Dennett, N. Shields, C. L. Peiris et al., "Motivational interviewing added to oncology rehabilitation did not improve moderate-intensity physical activity in cancer survivors: a randomised trial," *Journal of Physiotherapy*, vol. 64, no. 4, pp. 255–263, 2018.

[71] C. Ijsbrandy, W. H. van Harten, W. R. Gerritsen, R. P. M. G. Hermens, and P. B. Ottevanger, "Healthcare professionals' perspectives of barriers and facilitators in implementing physical activity programmes delivered to cancer survivors in a shared-care model: a qualitative study," *Supportive Care in Cancer*, vol. 28, no. 7, pp. 3429–3440, 2020.

[72] A. Henriksson, H. Igelström, C. Arving, K. Nordin, B. Johansson, and I. Demmelmaier, "The Phys-Can study: meaningful and challenging- supervising physical exercise in a community-based setting for persons undergoing curative oncological treatment," *Physiotherapy Theory and Practice*, vol. 38, no. 1, pp. 141–150, 2022.

[73] R. S. Beidas, B. Paciotti, F. Barg et al., "A hybrid effectiveness-implementation trial of an evidence-based exercise intervention for breast cancer survivors," *JNCI Monographs*, vol. 2014, no. 50, pp. 338–345, 2014.

[74] K. S. Courneya, "Exercise guidelines for cancer survivors: are fitness and quality-of-life benefits enough to change practice?" *Current Oncology*, vol. 24, no. 1, pp. 8-9, 2017.

[75] J. S. Holtrop, P. A. Estabrooks, B. Gaglio et al., "Understanding and applying the RE-AIM framework: clarifications and resources," *Journal of Clinical and Translational Science*, vol. 5, no. 1, p. e126, 2021.

[76] A. M. Husebø, S. M. Dyrstad, J. A. Søreide, and E. Bru, "Predicting exercise adherence in cancer patients and survivors: a systematic review and meta-analysis of motivational and behavioural factors," *Journal of Clinical Nursing*, vol. 22, no. 1-2, pp. 4–21, 2013.

[77] H. L. Ormel, G. G. F. van der Schoot, W. J. Sluiter, M. Jalving, J. A. Gietema, and A. M. E. Walenkamp, "Predictors of adherence to exercise interventions during and after cancer treatment: a systematic review," *Psycho-Oncology*, vol. 27, no. 3, pp. 713–724, 2018.

[78] C. S. Kampshoff, F. Jansen, W. van Mechelen et al., "Determinants of exercise adherence and maintenance among cancer survivors: a systematic review," *International Journal of Behavioral Nutrition and Physical Activity*, vol. 11, no. 1, p. 80, 2014.

[79] A. M. L. Husebø, B. Karlsen, H. Allan, J. A. Søreide, and E. Bru, "Factors perceived to influence exercise adherence in women with breast cancer participating in an exercise programme during adjuvant chemotherapy: a focus group study," *Journal of Clinical Nursing*, vol. 24, no. 3-4, pp. 500–510, 2015.

[80] K. S. Courneya, D. C. McKenzie, R. D. Reid et al., "Barriers to supervised exercise training in a randomized controlled trial of breast cancer patients receiving chemotherapy," *Annals of Behavioral Medicine*, vol. 35, no. 1, pp. 116–122, 2008.

[81] A. A. Kirkham, A. Bonsignore, K. A. Bland et al., "Exercise prescription and adherence for breast cancer: one size does not FITT all," *Medicine & Science in Sports & Exercise*, vol. 50, no. 2, pp. 177–186, 2018.

[82] J. C. Mewes, L. M. Steuten, M. J. Ijzerman, and W. H. van Harten, "Effectiveness of multidimensional cancer survivor rehabilitation and cost-effectiveness of cancer rehabilitation in general: a systematic review," *The Oncologist*, vol. 17, no. 12, pp. 1581–1593, 2012.

[83] B. E. Gubler-Gut, J. Pöhlmann, A. Flatz, M. Schwenkglenks, and S. Rohrmann, "Cost-effectiveness of physical activity interventions in cancer survivors of developed countries: a systematic review," *J Cancer Surviv*, vol. 15, no. 6, pp. 961–975, 2021.

[84] G. Early Breast Cancer Trialists' Collaborative, R. Peto, C. Davies et al., "Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials," *The Lancet*, vol. 379, no. 9814, pp. 432–444, 2012.

[85] K. Hefferon, H. Murphy, J. McLeod, N. Mutrie, and A. Campbell, "Understanding barriers to exercise implementation 5-year post-breast cancer diagnosis: a large-scale qualitative study," *Health Education Research*, vol. 28, no. 5, pp. 843–856, 2013.

[86] M. A. Kennedy, S. Bayes, R. U. Newton et al., "Implementation barriers to integrating exercise as medicine in oncology: an ecological scoping review," *J Cancer Surviv*, vol. 16, no. 4, pp. 865–881, 2022.

[87] Taskforce Cancer Survivorship Care, "Taskforce Cancer Survivorship Care [cited 2022 december 13th]," 2022, https://taskforcecancersurvivorshipcare.nl.

[88] W. G. Groen, M. R. ten Tusscher, R. Verbeek et al., "Feasibility and outcomes of a goal-directed physical therapy program for patients with metastatic breast cancer," *Supportive Care in Cancer*, vol. 29, no. 6, pp. 3287–3298, 2021.

[89] W. Heij, L. Sweerts, J. B. Staal et al., "Implementing a personalized physical therapy approach (Coach2Move) is effective in increasing physical activity and improving functional mobility in older adults: a cluster-randomized, stepped wedge trial," *Physical Therapy*, vol. 102, no. 12, Article ID pzac138, 2022.

[90] T. J. Waltz, B. J. Powell, M. E. Fernández, B. Abadie, and L. J. Damschroder, "Choosing implementation strategies to address contextual barriers: diversity in recommendations and future directions," *Implementation Science*, vol. 14, no. 1, p. 42, 2019 2019.

[91] G. Sheill, E. Guinan, L. O. Neill, D. Hevey, and J. Hussey, "The views of patients with metastatic prostate cancer towards physical activity: a qualitative exploration," *Supportive Care in Cancer*, vol. 26, no. 6, pp. 1747–1754, 2018.

[92] M. R. Ten Tusscher, W. G. Groen, E. Geleijn et al., "Physical problems, functional limitations, and preferences for physical therapist-guided exercise programs among Dutch patients with metastatic breast cancer: a mixed methods study," *Supportive Care in Cancer*, vol. 27, no. 8, pp. 3061–3070, 2019.

[93] L. Czosnek, J. Richards, E. Zopf, P. Cormie, S. Rosenbaum, and N. M. Rankin, "Exercise interventions for people diagnosed with cancer: a systematic review of implementation outcomes," *BMC Cancer*, vol. 21, no. 1, p. 643, 2021.

[94] A. Batra and W. Y. Cheung, "Role of real-world evidence in informing cancer care: lessons from colorectal cancer," *Current Oncology*, vol. 26, no. 11, pp. S53–S56, 2019.

[95] N. Ivers, G. Jamtvedt, S. Flottorp et al., "Audit and feedback: effects on professional practice and healthcare outcomes," *Cochrane Database of Systematic Reviews*, vol. 6, Article ID CD000259, 2012.

[96] M. L. McNeely, C. Sellar, T. Williamson et al., "Community-based exercise for health promotion and secondary cancer prevention in Canada: protocol for a hybrid effectiveness-implementation study," *BMJ Open*, vol. 9, no. 9, Article ID e029975, 2019.

[97] G. M. Curran, M. Bauer, B. Mittman, J. M. Pyne, and C. Stetler, "Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact," *Medical Care*, vol. 50, no. 3, pp. 217–226, 2012.