Exercise May Improve Completion of Standard and Emerging Cancer Treatments

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CATALÁ-VILAPLANA, I., S.E. CAO, K. ZADRAVEC, N. LEVASSEUR, R.J. KIMPLE, A.J. LIM, K.S. COURNEYA, and K.L. CAMPBELL. Exercise may improve completion of standard and emerging cancer treatments. *Exerc. Sport Sci. Rev.*, Vol. 53, No. 3, pp. 110–124, 2025. *Receipt of the entire course of intended anticancer treatment is critical to maximize treatment efficacy, reduce risk of disease recurrence, and improve survival. Engaging in an exercise program during cancer treatment has the potential to improve treatment completion, but standardization in terminology for reporting on cancer treatment completion is needed, especially as types of cancer treatments continue to evolve.*
Key Words: cancer treatment completion, relative dose intensity, medication adherence, exercise oncology, resistance training, aerobic training

KEY POINTS

- The receipt of full treatment dose as planned is considered a quality-of-care indicator in clinical oncology, but delivery of the target dose is not always achievable.
- Identification of new strategies, like exercise interventions, to improve the ability of an individual to receive as much of the intended dose as possible should be a priority.
- The majority of published studies that report on treatment completion outcomes focus on chemotherapy completion. More studies examining treatment completion of other cancer treatment types are needed.
- A wide variety of outcomes for treatment completion are used in exercise oncology studies and variable terms are used for similar outcomes. There is a need for standardization of terminology and definitions across the exercise oncology field.
- It is not clear whether higher levels of exercise improve treatment completion, or if improved tolerance of the cancer treatment enables an individual to more effectively participate in exercise.

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INTRODUCTION

Each year, nearly 20 million people globally are newly diagnosed with cancer (1), and millions more are living with a prior cancer diagnosis (2). Surgery, chemotherapy, and radiation therapy have been the three pillars of cancer treatment, although there have been recent advances in treatment approaches with the introduction of immunotherapy and targeted therapy (3,4). Systemic therapies (*i.e.*, chemotherapy, hormone therapy, immunotherapy, or targeted therapy) affect the whole body. Localized treatments (*i.e.*, surgery and radiation therapy) focus the tumor-destroying effect in a specific area (5). Systemic therapies and localized treatments can be used as a sole treatment method, in combination, such as in chemoradiation, or sequentially either before (neoadjuvant) or after (adjuvant) surgery (5).

The aim of cancer treatments can be to remove or reduce cancer cells (treatment with curative intent), extend survival (potentially life-prolonging treatment), or reduce symptom burden and improve quality of life without conferring a survival benefit (palliative treatment) (6). Although these treatments can decrease tumor and symptom burden, reduce recurrence

risk, and improve survival (7), they are associated with various side effects and toxicities including fatigue, pain, and chemotherapy-related peripheral neuropathy, as well as decreased muscular strength and cardiorespiratory fitness (8). These side effects can, in turn, reduce quality of life (QoL) and physical functioning for people living with and beyond cancer (5,7). Moreover, these side effects and toxicities may result in reductions, interruptions, or discontinuations of cancer treatments, which may reduce their efficacy. The general understanding in cancer care is that treatment effectiveness depends largely on an individual receiving as much of the intended dose as possible. However, optimal dose delivery is not always achievable (9).

Consistent evidence supports that exercise can be safe and well tolerated by most people during and after cancer treatments, and that exercise can help mitigate many adverse side effects related to treatment, enhance QoL, and improve physical function (10). This evidence has led to the development of cancer-specific exercise guidelines, which recommend first and foremost to "move more." To address common adverse side effects of cancer treatment, it is recommended to perform moderate-intensity aerobic exercise 2–3 times per week for 20–30 min, combined with resistance training 2 times per week, completing 2 sets of 8–15 repetitions for major muscle groups at moderate-to-vigorous intensity. Then, aim to meet the current physical activity guidelines for adults for overall health: at least 150–300 min·wk^{-1} of moderate-intensity aerobic exercise (or 75 min of vigorous-intensity aerobic exercise) combined with resistance training 2 times per week (10) (see Supplemental Digital Content 1, which shows the recommendations, http://links.lww.com/ESSR/A67). These guidelines are consistent with recommendations from the American Cancer Society (11) and supported by 2022 recommendations from the American Society of Clinical Oncology (ASCO), which state that oncology providers should recommend regular aerobic and resistance exercise during active treatment with curative intent, and may recommend preoperative exercise for people with lung cancer undergoing surgery (12).

Much less research has focused on the effects of exercise on cancer treatment completion, especially for treatments other than chemotherapy. A key question in the field of exercise oncology is if exercise can increase an individual's tolerance for the intended dose of planned treatments. This article will examine the potential of exercise to improve treatment completion for various types of cancer treatments, namely: chemotherapy, radiation therapy, chemoradiation, hormone therapy, immunotherapy, and targeted therapy.

HOW TO DEFINE TREATMENT COMPLETION

Treatment completion is a complex outcome that may vary by cancer type, disease stage, treatment modality, and treatment regimen. This review will outline treatment completion outcomes and definitions that have been used in exercise oncology studies examining the effect of exercise on treatment completion, or draw on outcomes used in treatment delivery studies, which potentially could be adapted for use in the exercise oncology field.

Systemic Therapy

For chemotherapy or chemoradiation regimens, treatment-related side effects can result in dose reductions (*e.g.*, change in amount of dose administered), dose delays (*e.g.*, change in timing of administration), a combination of both, or dose discontinuation (*e.g.*, the treatment is stopped) (13,14). Chemotherapy dose is typically based on body surface area or other anthropometric measures, which results in between-individual variation in dose prescribed (15). *Relative dose intensity (RDI)* is a single quantitative measure at the level of an individual that integrates dose reductions, delays, and discontinuations, and represents the actual dose intensity delivered as a percentage of the planned dose (16,17) (Fig. 1). The initially planned dose for cycle one typically forms the denominator, and this value is at the discretion of the treating oncologist based on clinical guidelines and clinical judgment (such as potential dose capping) (18). Specific to exercise intervention studies, the Exercise and Nutrition Interventions to Improve Cancer Treatment-Related Outcomes (ENICTO) collaborative research network has recently undertaken efforts to standardize the reporting approach for RDI. This has resulted in two suggested approaches: consider all drugs in any regime received throughout the entire chemotherapy treatment, or consider only drugs that are part of the first chemotherapy regime the treatment oncologist prescribes (19). The ENICTO approach also defines *dose reduction* as any reduction in the formula (mg·m^{-2}, mg·kg^{-1}) of at least 5% after the first cycle of chemotherapy administered, *dose delay* as any delay (*i.e.*, specific toxicity-related delays) of an individual drug >5 d, and *early stoppage* as the termination of at least one drug in a regimen before the intended number of cycles (19).

With chemotherapy, receipt of full treatment dose according to the planned treatment schedule is critical to improve treatment efficacy, reduce risk of disease recurrence, and improve survival (13). In people with colon cancer, an RDI < 60% is associated with an increased risk of early recurrence (20), whereas RDI >70% is associated with improved overall survival (21). Similarly, Kwak *et al.* (22) demonstrated that people with diffuse large-cell lymphoma receiving RDI ≤75% experienced significantly shorter survival (22–26). Likewise, clinical trials in breast cancer typically use an RDI ≥85% as a benchmark that is associated with improved chemotherapy effectiveness and better outcomes, even after 20 yr of follow-up (23–26). The survival benefit observed from receiving higher RDI has been supported by other observational studies in people with breast, lung, or ovarian cancer receiving chemotherapy (27–32).

Hormone therapy is most commonly used in the setting of breast and prostate cancers (33,34). Although treatment can also be delivered by intramuscular or subcutaneous injections, treatment completion is commonly reported as adherence to the oral medications. There is no standardized definition for medication adherence; it can be evaluated objectively or through self-report (35). Objective approaches such as pharmacy dispensing records or medication possession rate rely on dispensing data,

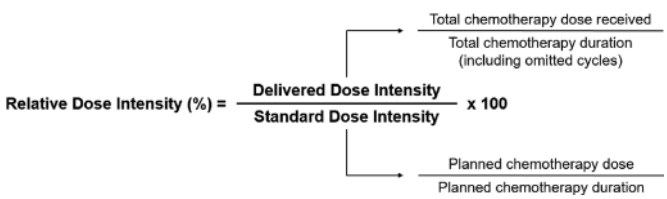

Figure 1. Relative dose intensity formula [Adapted from Schmitz *et al.* (18) Copyright © 2024, The Author(s) 2024. Published by Oxford University Press. Used with permission.]

with adherence defined as ≥80% (36). In contrast, self-reported adherence can be measured by questionnaires and pill diaries (37). For oral hormone therapy for breast cancer, self-report measures such as Morisky-Green (38) or VOILS-dose (39) are commonly used. Pill diaries are now used in most oral drug protocols, especially in larger cooperative group studies (40). In a systematic review examining adherence to adjuvant hormone therapy in breast cancer patients, Yussof *et al.* (41) defined medication adherence as receiving ≥80% of the prescribed medication within the intended timeframe. Non-adherence is defined as a treatment gap of more than 90 d, with a range of 60 to 180 d (41).

The approach to measuring treatment completion for immunotherapy and targeted therapy is currently inconsistent. Medication adherence to oral therapies have been used, like hormonal therapy. Clinically, treatment interruption is the metric that is most often used. In immunotherapy, interruption usually occurs due to disease progression or immune-related adverse events, and typically lasts for many weeks. For targeted therapies, interruption is most often related to toxicity from the on-target effects of the drug (*e.g.*, mucositis, diarrhea, rash).

Localized Treatments

Surgery is the main treatment for many cancers, either on its own or in combination with other treatment modalities. Although studies on surgical outcomes typically report on relevant clinical outcomes such as length of stay and postoperative complications (42–44), these are not a direct indication of treatment completion and are beyond the scope of this review. For reviews on preoperative exercise and surgical outcomes in a range of cancers, readers are directed to previous publications such as Molenaar *et al.* (43), Treanor *et al.* (45), and Waterland *et al.* (46).

For radiation therapy, treatment completion is typically measured by assessing radiation treatment breaks (47,48). Treatment breaks are defined as any unplanned discontinuation or interruption in radiation therapy dose, which result in the prolongation of the overall radiation treatment time (48). Treatment breaks greater than 1 wk are known to predict worse treatment outcomes in individuals receiving chemoradiation (49).

EXERCISE MECHANISMS TO ENHANCE TREATMENT COMPLETION

Although more research is needed to fully understand the mechanisms linking exercise to improved treatment completion outcomes, it is proposed that exercise may improve treatment completion through various pathways (Fig. 2). First, exercise has been shown to improve common treatment-related side effects and toxicities in people undergoing systemic or localized treatments (*e.g.*, fatigue), which may improve tolerance to the treatments and translate into improved cancer treatment completion rates (50,51). Second, body composition factors may influence treatment completion. Excess adiposity (*i.e.*, larger visceral or intramuscular adiposity) has been associated with lower RDI and worse breast cancer–specific survival (52). Similarly, sarcopenia (low muscle mass) at diagnosis and muscle loss due to cancer and cancer treatments have also been associated with lower RDI and higher overall mortality (53). Exercise during treatment could improve RDI through exercise-induced reductions in fat mass and preservation of lean mass, improving, in turn, the pharmacokinetic properties of chemotherapy (19).

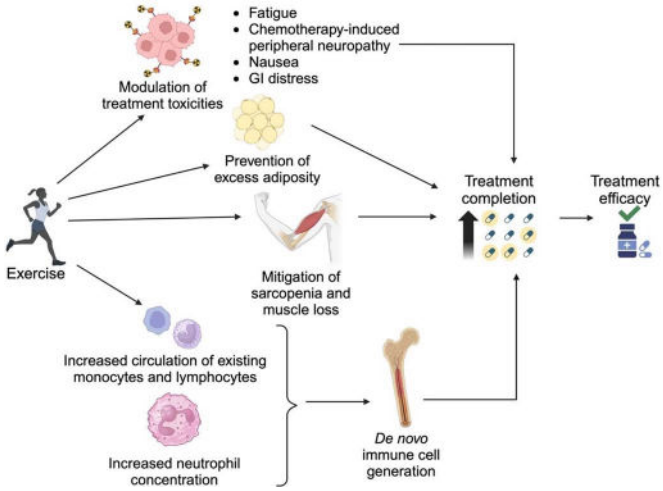

Figure 2. Exercise mechanisms to enhance treatment completion.

Third, exercise may also improve treatment completion through maintenance and/or stimulation of immune cell production (54). Exercise promotes the mobilization, redistribution, activation, and infiltration of immune cells (*i.e.*, natural killer cells, monocytes, and cytotoxic T cells) by increasing blood flow (55,56). Neutrophil concentration also increases during exercise and the recovery period (57,58). The exercise-mediated mobilization and redistribution of immune cells stimulate the bone marrow to initiate *de novo* immune cell generation (*i.e.*, production of new immune cells) (59). This may explain why people with cancer engaging in exercise training are less likely to have dose reductions due to low immune cell numbers (54), leading to improved treatment completion. These proposed effects may be impacted by tumor site, treatment regimen, and individual factors (9), but the normalizing properties of exercise have been suggested to enhance cancer treatment completion, and consequently treatment efficacy (60). However, it is of note that questions remain around the direction of causal inference. Based on the currently available evidence, it is not clear whether higher levels of exercise or engagement in exercise improves treatment completion, or if improved tolerance of the treatment (*i.e.*, allowing for higher treatment completion) allows an individual to be more capable of participating in exercise.

METHODS USED TO EXAMINE THE EFFECT OF EXERCISE ON TREATMENT COMPLETION

To investigate the effect of exercise on treatment completion for various types of cancer treatments, a comprehensive search of existing literature was conducted. Included studies were those that (i) enrolled adults (≥18 yr old) who were receiving curative intent, potentially life-prolonging, or palliative cancer treatment (*i.e.*, chemotherapy, radiation therapy, chemoradiation, hormone therapy, immunotherapy, or targeted therapy) for any cancer stage and any cancer type; (ii) delivered an intervention involving aerobic and/or resistance exercise (*i.e.*, single-arm, nonrandomized, or randomized controlled trials); and (iii) assessed treatment completion. Preclinical studies and interventions specifically focused on behavior change, mind-body exercise interventions (*e.g.*, yoga, Pilates, Tai Chi), or therapeutic exercise interventions (*e.g.*, postsurgical rehabilitation, range of

motion exercises) were not included in this review. Gray literature repositories were hand-searched for studies that reported on relevant outcomes.

Treatment completion outcomes that were included were those related to the dosage and timing of treatment. In the literature, other factors grouped under treatment completion may also be reported—most commonly, treatment toxicities (*e.g.*, neutropenia, fatigue, nausea) (61,62) and health care resource utilization (*e.g.*, length of stay, hospital readmission) (63–65), but are beyond the scope of this review.

The potential of exercise to improve clinical and patient reported outcomes in the context of the modern cancer treatment landscape has recently been outlined by Courneya *et al.* (66) in "Exercise Across the Post Diagnosis Cancer Continuum (EPiCC)." This framework addresses how exercise could be integrated as part of cancer treatment and supportive care from diagnosis to death. This is particularly salient with the increasing complexity of cancer care as newer treatment types (*i.e.*, immunotherapy and targeted therapies) are being delivered alongside standard treatments (*i.e.*, surgery, chemotherapy, radiation therapy, and hormone therapy) (67). Lower relapse rates and improved survival make supportive care an integral part of cancer care. The key proposition of the EPiCC Framework is that the effects of exercise on any outcome, including cancer treatment completion, may depend on the combination and sequencing of those cancer treatments. In line with the EPiCC Framework, this review examines the effect of exercise as supportive care during treatment (*i.e.*, intrahabilitation). Any studies that include a pretreatment phase will be termed neoadjuvant, as opposed to the term "prehabilitation" that is used in the EPiCC Framework to prevent confusion with preoperative interventions.

Although a systematic search has been undertaken, this article is not a systematic review and the results are presented in a narrative review. A few key reasons have informed this strategy. First, due to inconsistencies with terminology, creating a comprehensive search strategy that could locate all relevant studies was a significant challenge. Second, as a perspective for progress, this review wanted to capture the state of the field as it stands and propose directions for the future. Because studies in progress or awaiting publication are not well captured in a systematic review, it was appropriate to diverge.

Although general definitions of treatment completion outcomes were outlined earlier, a variety of terms have been used to describe these outcomes in the exercise oncology literature. For example, "chemotherapy dose delay" has also been described by authors as "cycle deferral" or "treatment delay." For this review, the various treatment completion terms from the identified studies have been unified into a standardized treatment completion outcome (*e.g.*, "dose delay" encompasses both "cycle deferral" and "treatment delay") and summarized in Table 1. All treatment completion results from the identified studies have been reported using these standardized terms. Chemoradiation has not been

TABLE 1. Treatment completion outcomes used in included exercise studies and proposed definitions for future use.

Standardized Outcome	Terms Used in Included Studies	Standardized Definitions Proposed for Future Use
Chemotherapy		
Relative dose intensity	- Relative dose intensity - Average dose intensity	Represents the actual delivered dose intensity as a fraction of the planned dose intensity of the chemotherapy regimen (Weycker *et al.*, 2012; (16))
Dose reduction	- Dose reduction	Any reduction in the formula ($mg \cdot m^{-2}$, $mg \cdot kg^{-1}$) of at least 5% after the first cycle administered (Schmitz *et al.*, 2025; (18))
Dose delay	- Dose delay - Treatment delays - Cycle deferral	Any delay or a specific toxicity-related delay of any individual drug >5 d (Schmitz *et al.*, 2025; (18))
Early stoppage	- Early discontinuations - Chemotherapy discontinuation - Chemotherapy stoppage	Termination of at least one drug in a regimen before the intended number of cycles (Schmitz *et al.*, 2025; (18))
Medication adherence[a]	- Treatment adherence - Treatment tolerance and compliance	Adherence as tracked by medical records of attendance (Arthuso *et al.*, 2021; (86)). Oral chemotherapies may refer to hormone therapy or targeted therapy adherence
Receipt of full dose	- Chemotherapy completion - Completion rate - Receipt of planned dose - Dose intensity -Treatment completion	Number of individuals who receive the full treatment dose (100%) over the intended timeframe as per the original treatment protocol (*i.e.*, no dose reductions, dose delays, or early stoppage) (Christodoulidis *et al.*, 2023; (83))
Radiation therapy		
Radiation treatment breaks	- Radiation therapy interruption	Unplanned discontinuation or interruption in radiation therapy dose (Shaikh *et al.*, 2016; (49))
Relative dose intensity[a]	- Dose intensity	Represents actual delivered dose intensity as a fraction of the planned dose intensity of the radiation therapy regimen (Fig. 3)
Hormone therapy		
Medication adherence	- Medication adherence	Having a medication supply of ≥80% of the prescribed medication during a given time period (Yussof *et al.*, 2022; (41))
Immunotherapy		
Dose delay	- Dose delay - Treatment interruption	Any interruption to the medication schedule, usually considered anything >7 d in clinical practice
Treatment discontinuation[a]	- Treatment discontinuation	Termination of at least one drug in a regimen before the intended number of cycles (Schmitz *et al.*, 2025; (18))
Targeted therapy		
Dose reduction[a]	- Dose reduction	Any reduction in the formula of at least 5% after the first cycle administered (Schmitz *et al.*, 2025; (18))
Treatment discontinuation[a]	- Treatment discontinuation	Termination of at least one drug in a regimen before the intended number of cycles (Schmitz *et al.*, 2025; (18))
Medication adherence[a]	- Treatment adherence	Adherence to the medication schedule as measured by dispensing data, pill counts and/or pill diaries, defined as ≥80% of the intended doses received (O'Sullivan *et al.*, 2021; (40))

[a] Outcomes currently listed in exercise protocols or ongoing studies.

included as a stand-alone treatment type because all treatment completion outcomes for chemoradiation can be categorized as either chemotherapy completion or radiation completion outcomes.

EFFECTS OF EXERCISE ON TREATMENT COMPLETION

A total of 30 studies investigated the effect of an exercise intervention on treatment completion (Table 2). The majority reported on chemotherapy (n = 23; 76.7%), with other studies in chemoradiation (n = 4; 13.3%) (67–70) and hormone therapy (n = 3; 10.0%) (71–73). No studies were identified that assessed the effect of exercise on treatment completion for radiation therapy alone (*i.e.*, not combined with chemotherapy), immunotherapy, or targeted therapy. Most studies have been undertaken in people with breast cancer (n = 11; 37.9%) (61,65,67,71–78), followed by colorectal cancer (n = 5; 17.2%) (68,79–82) and esophagogastric cancer (n = 4; 13.8%) (54,63,83,84). A treatment completion outcome was specified as a primary outcome in three studies (10.3%), all of which examine the effect of exercise during chemotherapy (77,79,85). Twelve published protocols with treatment completion outcomes were identified (Table 3) (86–97). Only one of the protocols listed treatment completion as the primary outcome (97).

Chemotherapy

Of the 23 chemotherapy studies identified, 11 studies (47.8%) (63,74,78,80,83,85,98–102) reported a significant benefit of exercise on treatment completion outcomes. Among the 13 studies that assessed treatment completion using RDI, 3 studies (23.1%) reported a significant benefit of exercise (74,99,101). Ten studies did not show a significant benefit, including the two studies that had RDI as a primary outcome (77,79).

In the START study, people with stage I to IIIA breast cancer were randomly assigned to supervised aerobic (n = 78) or resistance (n = 82) exercise, or usual care (n = 82) for the duration of chemotherapy (median: 17 wk) (74). Participants in the resistance exercise group achieved a higher RDI compared to participants in the usual care group (89.8% vs 84.1%, respectively; P = 0.033). There was no significant difference in RDI between participants in the aerobic exercise group versus the control group (87.4% vs 84.1%, respectively; P = 0.266). Likewise, in a single-arm, nonrandomized pilot study by Mizrahi *et al.* (101), people with recurrent stage I to IV ovarian cancer (n = 21) underwent 12 wk of supervised/home-based aerobic/resistance exercise during chemotherapy. Participants who completed the exercise intervention achieved a significantly higher RDI compared to individuals who withdrew from the study and who did not complete the exercise intervention (94.6% vs 79.8%, respectively; P = 0.030). Lastly, in a single-arm study by Chiarotto *et al.* (99), people with stage IV cancer (n = 35) attended supervised aerobic and resistance training once per week during palliative chemotherapy, where the duration of the exercise intervention was based on participant preference (median: 16 wk). Again, the study was not randomized, and all participants received the exercise intervention. Treatment completion was only assessed for people with metastatic colorectal cancer (n = 12) or multiple myeloma (n = 3). Specifically, RDI was compared between study participants and age- and sex-matched "nonparticipants." It is unclear if these "nonparticipants" were enrolled and then withdrew from the study, or if they were not recruited for/enrolled in the study at all. Compared to age- and sex-matched nonparticipants, people with metastatic colorectal cancer received a significantly higher RDI (96.0% vs 86.0%, respectively; P = 0.035). However, there was no significant difference in RDI for people with metastatic multiple myeloma and nonparticipants (100% vs 98.0%, respectively). Treatment completion was not a primary outcome of any of these studies.

In contrast, in the FORCE study, Caan *et al.* (79) did not find a significant difference in RDI between people with stage II to III colon cancer who were randomly assigned to home-based resistance exercise (n = 90) or usual care (n = 91) during chemotherapy (3 to 6 months). This study examined treatment completion as a primary outcome. RDI did not significantly differ between participants in the resistance exercise group versus control group (79.0% vs 82.0%, respectively; estimated mean difference: −0.04; P = 0.19). Although females in the resistance training group did not experience higher RDI in comparison with females in the usual care group (78.0% vs 76.0%, respectively; estimate mean difference: 0.02, 95% CI: −0.07 to 0.10), males in the usual care group achieved a higher mean RDI compared to males in the resistance training group (87.0% vs 80.0%, respectively; estimate mean difference: −0.09, 95% CI: −0.16 to −0.02). Based on the sex subgroup analysis, sex and resistance training showed an interaction P value of 0.07, which approaches significance. The authors propose several explanations for the lack of benefit from home-based resistance exercise on RDI in their study. First, the small increase in muscle mass seen with the resistance exercise intervention group may have not been sufficient to improve RDI. Second, the format of the resistance exercise intervention may not have been adequate to significantly change RDI, such as home-based resistance training being less effective than a supervised setting, or insufficient frequency or intensity of the resistance training program. Overall, the authors indicate that future research is needed to understand the pharmacokinetic properties of combination chemotherapy regimens for different body compositions and how these pharmacokinetic properties may be affected by changing body composition through exercise and diet (79).

Similar results were seen in the LEANER study by Sanft *et al.* (77), the other study with RDI as a primary outcome. In the LEANER study, people with stage I to III breast cancer were randomly assigned to an exercise/nutrition counseling intervention (n = 87) or usual care (n = 86) during chemotherapy. The exercise/nutrition counseling intervention consisted of in-person or virtual counseling sessions delivered for 3 months. The number of sessions delivered during chemotherapy depended on participants' chemotherapy duration. The aim of the exercise counseling sessions was for participants to reach at least 150 min·wk^{-1} of moderate-to-vigorous intensity physical activity, or at least 75 min·wk^{-1} of vigorous intensity physical activity, as well as resistance exercise twice per week. RDI did not significantly differ between participants in the exercise/nutrition intervention versus control group (93.0% vs 94.0%, respectively; P = 0.69). The proportion of participants in the exercise/nutrition group who achieved an RDI of ≥85% compared to those in the control group also did not significantly differ (81.0% vs 85.0%, respectively; P = 0.44).

Treatment completion was also evaluated through outcomes other than RDI, namely, dose reductions, dose delays, and early stoppage. These outcome measures were reported in 10 studies (61,65,76–78,80,98,100,102,103). Of these 10 studies, 5 studies

TABLE 2. Effects of exercise on cancer treatment completion.

First Author, Year	Cancer Type	Study Arms	Intervention	Exercise Prescription	Exercise Adherence	Results
Chemotherapy						
Allen et al. (2022; (63))	Esophagogastric (locally advanced, neo-adj)	EX = 26 UC = 28	Sup 2× a week and HB 3× a week, 15 wk total + nutrition/psych	AeT: 25 min, 40%–60% HRR, RPE 11–14 ReT: 2 × 12 reps, RPE 12–14	Attendance: 76% ± 14% (sup), 65% ± 27% (HB)	↑ Receipt of full dose EX vs UC[a]
Bausys et al. (2023; (88))	Gastric (stages I–IV)	EX = 61 UC = 61	HB AeT 7× a week and ReT 3× a week during chemo + nutrition/psych	AeT: 10–30 min, 40%–65% HRR ReT: 10–20 min	NR	↓ Dose reduction EX vs UC[a] ↓ Early stoppage EX vs UC[a]
Brouwer et al. (2024)[e]	Ovarian (stages I–IV)	EX = 40 UC = 41	Comb sup AeT and ReT 2× a week + nutrition counseling	AeT: 30 min, 50%–80% maximal workload ReT: 2 × 10 reps, 70%–80% 1-RM	Median attendance: 71.7% Mean exercise RDI: 72.6%	↑ RDI EX vs UC[d]
Caan et al. (2024; (79))	Colon (stages II–III)	EX = 90 UC = 91	HB ReT 2× a week during chemo (3–6 mos)	3–5 × 6–10 reps, 65%–85% 1-RM	Median frequency: 1.4× a week Median intensity: 62% 1-RM Median volume: 3 × 7.5 reps	↔ RDI[b] ↑ *n* with <85% RDI EX vs UC[a]
Chiarotto et al. (2017; (99))	Mixed (stage IV)	EX = 35 (vs nonparticipants)	Sup AeT and ReT 1× a week Indefinite; lasted as long as participant wished	AeT: up to 45 min ReT: 2 × 10 reps	Median 16 classes attended (range: 1–89) Adherence: 73.1%	↑ RDI EX vs nonparticipants[a,c]
Christensen et al. (2018; (54))	Esophagogastric (stages 0–III, neo-adj)	EX = 21 UC = 29 (non-rand)	Sup AeT and ReT 2× a week during chemo (range: 19–39 sessions)	AeT: 31–38 min HIIT ReT: 3 × 8–12 reps	Attendance: 68.7% Sessions with dose reduction or early termination: 25.8%	↔ Dose reduction
Christodoulidis et al. (2023; (83))	Esophago-gastric (stages I–IV, neo-adj)	EX = 47 UC = 45 (non-rand)	HB exercise program (mean = 12 wk) + nutrition	150 min mod intensity a week	NR	↑ Receipt of full dose EX vs UC[a]
Courneya et al. (2007; (74))	Breast (stages I–IIIa)	AeT = 78 ReT = 82 UC = 82	Sup AeT 3× a week and ReT 2× a week during chemo (median = 17 wk)	AeT: 15–45 min, 60%–80% $\dot{V}O_{2max}$ ReT: 2 × 8–12 reps, 60%–70% 1-RM	AeT: 95.6% (duration), 87.2% (intensity) ReT: 96.8%	↑ RDI AeT and ReT vs UC[a] ↔ *n* with ≥85% RDI
Courneya et al. (2009)[f]	Lymphoma (stages I–IV)	AeT = 60 UC = 62	Sup AeT 3× a week, 12 wk total	15–45 min, 60%–75% $\dot{V}O_{2peak}$	Attendance: 77.8% Duration: 99.0% Intensity: 90.7%	↔ Planned minimum cycles ↔ Planned maximum cycles
Courneya et al. (2013; (75))	Breast (stage I–IIIc)	STAN = 96 COMB = 104 HIGH = 101	Sup AeT and ReT 3× a week during chemo (mean = 16.4 wk)	STAN: AeT (25–30 min, 55%–75% $\dot{V}O_{2peak}$) COMB: AeT (25–30 min, 55%–75% $\dot{V}O_{2peak}$) + ReT (2 × 10–12 reps, 60%–75% 1-RM) HIGH: AeT (50–60 min, 55%–75% $\dot{V}O_{2peak}$)	Attendance: 87.8% (STAN), 78.5% (COMB AeT), and 66.0% (COMB ReT), 81.6% (HIGH) Mean intensity ($\dot{V}O_{2peak}$): 68.4% (STAN), 67.4% (COMB), 65.2% (HIGH)	↔ RDI ↔ *n* with ≥85% RDI
Gonçalves et al. (2024; (100))	Gastric (locally advanced, vneo-adj)	EX = 22 UC = 17	HB AeT, ReT, and IMT pre-op and 30 d post-op	NR	87.5% (AeT), 50.0% (ReT), 26.5% (IMT)	↓ Dose delay EX vs UC[a,d] ↓ Dose reduction EX vs UC[a,d]
Iyengar et al. (2024; (61))	Breast (stages I–IIIc)	EX = 72 UC = 72	Sup AeT 3× a week during chemo, after chemo, during/after chemo	AeT 20–50 min, 55%–100% $\dot{V}O_{2max}$	Median adherence: 77%	↔ RDI ↔ Dose reduction ↔ Dose delay ↔ Early stoppage
Kirkham et al. (2020; (76))	Breast (stages I–IIIa)	EX = 73 UC = 85 (historical cohort)	Sup AeT and ReT 3× a week during chemo	AeT: 20–30 min, 50%–75% HRR ReT: 1–2 × 10–12 reps, 50%–70% 1-RM	Frequency: 64% ± 25% Intensity: 73% ± 20% Duration: 82% ± 20% ReT: 57% ± 23%	↔ Dose reduction ↔ Dose delay ↔ RDI ↔ *n* with <85% RDI
Mijwel et al. (2020; (65))	Breast (stages I–IIIa)	AT-HIIT = 80 RT-HIIT = 79 UC = 81	Sup AeT and ReT 2× a week, 16 wk total	AT-HIIT: 20 min RPE 13–15, 3 × 3 min RPE 16–18 RT-HIIT: 2–3 × 8–12 reps 70%–80% 1-RM, 3 × 3 min RPE 16–18 AeT	Attendance: 68.0% (RT-HIIT), 63.0% (AT-HIIT) Adherence: 83.0% (RT-HIIT), 75.0% (AT-HIIT)	↔ Dose reduction ↔ RDI ↔ *n* with ≥85% RDI
Mizrahi et al. (2015; (101))	Ovarian (recurrent, stages I–IV)	EX = 21 UC = 9 (nonparticipants)	1× a week sup and 3—4× a week HB AeT and ReT, 12 wk total	AeT: 10–40 min, 55%–70% HR_{max} (RPE 11–14) ReT: 10–40 min, 50%–70% 1-RM	Adhered to 90 min·wk^{-1} target 81.0%	↑ RDI EX vs UC[a]
Okada et al. (2022; (85))	Pancreatic (stages I–III)	EX = 38 (historical cohort)	Sup AeT and ReT for POD1 to DC and during chemo	AeT: 20–60 min, 85% HRR ReT: 4 × 10 reps	Attendance: 88%	↑ Receipt of full dose EX vs historical cohort[a,b]
Sanft et al. (2023; (77))	Breast (stages I–III)	EX = 87 UC = 86	Exercise/nutrition counseling; 4× a week for 1 mos., 2× biweekly for months 2–3, 1× a month thereafter	AeT: 150 min·wk^{-1} MVPA or 75 min·wk^{-1} vigorous-intensity ReT: 2× a week	52.0% were meeting PA guidelines post-intervention	↔ RDI[b] ↔ *n* with ≥85% RDI ↔ Dose reduction ↔ Dose delay
Shim et al. (2019; (80))	Colorectal (stages I–III)	EX = 25 UC = 14 (non-rand)	Sup AeT 3× a week during chemo	50 min, RPE 11–14	NR	↓ Dose reduction EX vs UC[a]

Continued next page

TABLE 2. *(Continued)*

First Author, Year	Cancer Type	Study Arms	Intervention	Exercise Prescription	Exercise Adherence	Results
Simonsen et al. (2020; (84))	Esophagogastric (stages I–III)	EX = 27 UC = 35 (non-rand)	Sup AeT and ReT 2× a week, 12 wk total	AeT: 20 min 60%–70% HR_{max} + 4 × 4 min 75%–95% HR_{max} ReT: 3 × 8–12 reps, 50%–80% 1-RM	Attendance: 69.0% AeT adherence: 90.4% ReT adherence: 76.6%	↔ RDI
Thomsen et al. (2024; (102))	Colorectal (liver metastases)	EX = 22 UC = 12	5× a week HB AeT, 8 wk	AeT: 30–50 min, low to high intensity using RPE and HR_{max}	Median attendance: 93% Median adherence: 66%	↓ Dose delay EX vs UC[a] ↑ RDI EX vs UC ↓ Dose reduction EX vs UC ↓ Early stoppage EX vs UC
Van Vulpen et al. (2016; (82))	Colon (stage M0)	EX = 15 UC = 13	2× a week sup AeT and ReT + 3× a week HB exercise, 18 wk total	AeT: 60 min, HR at/below VT ReT: 2 × 10 reps, 65%–75% 1-RM	Attendance: 89.0%	↔ RDI ↔ *n* with ≥85% RDI
Van Waart et al. (2015; (78))	Breast (stages I–III)	EX = 77 PA = 76 UC = 77	EX: 5× a week HB AeT and 2× a week sup AeT/ReT during chemo PA: 5× a week HB	AeT: 30 min, 50%–80% HR_{max} ReT: 2 × 8 reps, 80% 1-RM PA: >30 min, RPE 12–14	Attendance: 71.0%	↓ Dose reduction EX vs PA and UC[a]
Van Waart et al. (2018; (81))	Colon (stage II–IV)	EX = 7 PA = 8 UC = 8	EX: 2× a week sup AeT and ReT, HB 5× a week during chemo PA: 5× a week HB	AeT: 30 min, 50%–80% HR_{max} ReT: 2 × 8 reps, 80% 1-RM PA: >30 min, RPE 12–14	Attendance: 61%	↔ Receipt of full dose
Chemoradiation						
Carayol et al. (2019; (67))	Breast (stages I–III)	EX = 72 UC = 71	Sup/HB AeT/ReT 3× a week during chemoradiation (26 wk) + nutrition	AeT: 30–45 min at 50%–75% HR_{max} ReT: 2–5 × 6–12 reps	Mean attendance: 67% AeT adherence: 71% ReT adherence: 58%	↔ RDI
Dewberry et al. (2019; (69))	Esophageal (locally advanced, neo-adj)	EX = 11 UC = 11 (non-rand)	Sup multimodal prehabilitation (physical, nutritional, psych) during chemoradiation (4–6 wk)	NR	NR	↔ Chemotherapy dose reduction
Morielli et al. (2021; (68))	Rectal (stages IIa–IVa, neo-adj)	EX = 18 UC = 18	Sup AeT 3× a week during chemoradiation HB MVPA after chemoradiation	AeT 28–40 min, including 5–8 × 2 min at 85% $\dot{V}O_{2peak}$ 150 min·wk^{-1} MVPA after chemoradiation	Median attendance: 82%	↔ Radiation dose ↔ *n* with >80% planned chemo dose
Xu et al. (2015; (70))	Esophageal (locally advanced, neo-adj)	EX = 30 UC = 29	Sup AeT 3× a week, 4–5 wk total + nutrition	25 min, 60% HR_{max}	Attendance: 68% (range: 32%–100%)	↔ Chemotherapy dose reduction ↔ Early stoppage ↔ Radiation treatment break
Hormone therapy						
Irwin et al. (2015; (71))	Breast (stage 0–III)	EX = 61 UC = 60	Sup ReT 2× a week and HB AeT 150 min·wk^{-1}, 52 wk total	AeT: 150 min·wk^{-1}, 50%–80% HR_{max} ReT: 3 × 8–12 reps	Mean increase in PA = 159 min·wk^{-1}; completed mean 70% ReT sessions	↔ Self-reported medication adherence
Myers et al. (2022; (72))	Breast (stages I–III)	EX = 27	Sup ReT 2× a week and HB AeT 1–3× a week, 6 wk total	AeT: 30–60 min ReT: 1–3 × 8–15 reps, RPE 6–8/10	Attendance: 91%	↔ Self-reported medication adherence
Tamaki et al. (2018; (73))	Breast (stage NR)	EX = 102 UC = 37	HB PA for 120–150 min·wk^{-1}, 52 wk total	120–150 min·wk^{-1} PA	NR	↑ Self-reported medication adherence EX vs UC[a,d]

[a]Significant result.

[b]Stated as primary outcomes.

[c]Treatment completion only determined for patients with colorectal cancer and multiple myeloma, only significant for patients with colorectal cancer.

[d]Preliminary results reported in abstract only.

[e]Brouwer CG, Hartman Y, Stelten S, et al. Clinical Outcomes Of A Combined Exercise And Dietary Intervention In Patients With Ovarian Cancer: 1646. *Medicine & Science in Sports & Exercise*. 2024 Oct;56(10S):555.

[f]Courneya KS, Sellar CM, Stevinson C, et al. Randomized Controlled Trial of the Effects of Aerobic Exercise on Physical Functioning and Quality of Life in Lymphoma Patients. *JCO*. 2009 Sep 20;27(27):4605–12.

1-RM, 1-repetition maximum; AeT, aerobic training; AT-HIIT, high-intensity aerobic training; COMB, combined aerobic and resistance training; DC, discharge; EX, exercise; HB, home-based; HIGH, high-dose aerobic exercise prescription; HIIT, high-intensity interval training; HR_{max}, maximum heart rate; HRR, heart rate reserve; IMT, inspiratory muscle training; mod, moderate intensity; mos, months; neo-adj, neo-adjuvant; non-rand, not randomized; NR, not reported; PA, physical activity; POD1, day 1 postoperative; psych, psychological; PT, physical therapy; RDI, relative dose intensity; ReT, resistance training; RPE, rating of perceived exertion; RT-HIIT, resistance training with high-intensity aerobic training; STAN, standard aerobic exercise prescription; Sup, supervised; UC, usual care; $\dot{V}O_{2max}$ and $\dot{V}O_{2peak}$, maximum aerobic capacity.

(50.0%) reported a significant benefit of exercise (78,80,98,100,102). In people with stage I to IV gastric cancer who were randomly assigned to home-based aerobic/resistance exercise (*n* = 61) or usual care (*n* = 61) during chemotherapy, Bausys *et al.* (98) reported that significantly lower proportion of patients in the exercise group required dose reductions (5.7% vs 23.5%, respectively;

TABLE 3. Protocols expected to report on the effect of exercise on cancer treatment completion.

First Author, Year	Cancer Type	Target Study Size, Treatment Arms	Treatment Type	Intervention	Outcomes Measured	Expected Completion
Arthuso et al. (2021; (86))	Non-muscle invasive bladder (clinical stage cis, Ta, or T1)	*n* = 66 2 arms	Intravesical therapy (immunotherapy and/or chemo)	Sup HIIT 3× a week, 12 wk	Medication adherence[b]	August 2024
Berntsen et al. (2017; (96))	Breast, colorectal, prostate	*n* = 600 4 arms (2 × 2 factorial design)	Neo-adj or adj chemo, endocrine therapy, adj rad therapy, adj endocrine, rad w/ curative intent w/o endocrine therapy	Sup exercise for 6 mos. AeT and ReT at low-mod or high intensity + behavior change techniques	Receipt of full dose	Primary completion December 2024
Boniface et al. (2022; (91))	Breast (stages I–III)	*n* = 712 2 arms	Neo-adj chemo	HB HIIT & ReT 2× a week	RDI	Primary completion December 2025
Daviu Cobián et al. (2024; (88))	Epithelial ovarian cancer (stages III and IV, ≥70 yr)	*n* = 216 2 arms	Neo-adj chemo	Sup ReT 2× a week, HB AeT	Treatment completion	NR
Grigoletto et al. (2023; (89))	Lung or head and neck (all stages)	*n* = 40 2 arms	Chemo a/o radiation	Sup HB ReT 2× a week and AeT 20 min·d^{-1}	Treatment completion	NR
Hayes et al. (2023; (87))	Ovarian (all stages)	*n* = 500 2 arms	Chemo	HB mod mixed-mode, 450 METs·wk^{-1}	RDI	Primary completion December 2024
Joly et al. (2020; (93))	Mixed (metastatic)	Phase II *n* = 120 Phase III *n* = 312 2 arms	First- or second-line oral targeted therapy w/o chemo	Sup HB ReT 1× a week, HB AeT 2× a week, 12 wk	Medication adherence	Primary completion October 2024
Kjeldsted et al. (2023; (90))	Breast (all stages)	*n* = 120 2 arms	Neo-adj chemo	Sup HIIT and ReT 3× a week, 24 wk	Dose reductions, dose delays, treatment discontinuation, RDI	Primary completion February 2024
Luo et al. (2021; (92))	Pancreatic (all stages, borderline resectable or locally advanced)	*n* = 40 2 arms	Neo-adj chemo w/ or w/o rad	Sup ReT and AeT 2× a week, up to 6 mos	RDI	NR
Mikkelsen et al. (2018; (95))	Pancreatic, biliary tract, or lung (locally advanced or metastatic, unresectable)	*n* = 100 2 arms	First-line chemo, immunotherapy, or targeted therapy	Sup ReT 2× a week, HB AeT, 12 wk + nutrition and counseling	Dose reduction[b] Treatment discontinuation	Primary completion July 2020
Roy et al. (2016; (97))	Gastro-esophageal (all stages)	*n* = 120 2 arms	Perioperative chemo	Sup AeT and ReT 3× a week, 18 sessions + nutrition and psych	Receipt of full dose[a]	Primary completion March 2018
Tully et al. (2020; (94))	Esophagogastric (all stages)	*n* = 62 2 arms	Neo-adj chemo	Sup or HB ReT and AeT, 2–3× a week, throughout tx	Medication adherence	Primary completion December 2020

[a]Stated as primary outcomes.

[b]Measurement of outcome not specified, unclear how this will be quantified and in which treatments

adj, adjuvant; a/o, and/or; AeT, aerobic training; chemo, chemotherapy; HB, home-based; HIIT, high-intensity interval training; mod, moderate, mos, months; neo-adj, neo-adjuvant; psych, psychological intervention; rad, radiation therapy; ReT, resistance training; sup, supervised; tx, treatment; w/, with; w/o, without.

P = 0.012) or early stoppages (1.9% vs 13.7%, respectively; P = 0.031). In a nonrandomized controlled trial by Shim *et al.* (80), people with stage I to III gastric cancer were assigned in order of enrollment to supervised aerobic exercise (n = 25) or usual care (n = 14) during chemotherapy. Significantly fewer participants in the exercise group required dose reductions or early stoppage compared to the control group (12.8% vs 20.5%, respectively; P = 0.018). The PACES study randomly assigned people with stage I to III breast cancer to low-intensity physical activity (n = 76), moderate-intensity aerobic/resistance exercise (n = 77), or usual care (n = 77) during chemotherapy (78). Significantly fewer participants in the moderate-intensity aerobic/resistance exercise group had dose reductions compared to those in the low-intensity physical activity and control groups (12.0% vs 34.0% vs 34.0%, respectively; P = 0.002). Preliminary results of the ongoing PROTECT study demonstrate a benefit of exercise on chemotherapy completion (100). People with locally advanced and potentially resectable gastric cancer were randomly assigned to home-based aerobic/resistance exercise and inspiratory muscle training (n = 22) or usual care (n = 17) during neoadjuvant chemotherapy with curative intent. Compared to those in the control group, participants in the home-based aerobic/resistance exercise group had significantly fewer dose reductions (12.5% vs 87.5%, respectively; P < 0.05) and dose delays (23.1% vs 66.7%, respectively; P < 0.05) in chemotherapy. Lastly, Thomsen *et al.* (102) found that individuals with advanced colorectal cancer presenting with liver metastases who participated in exercise had lower relative risk for dose delays than the control group (RR 0.48, 95% CI: 0.23–0.99). This RCT randomized individuals to a postoperative exercise protocol of home-based aerobic exercise on a cycle ergometer five times per week, for a total of 8 wk. Duration and intensity increased throughout the study, ranging from 30 to 50 min of low-to-high intensity, determined by RPE or a percentage of maximum heart rate. Measures of RDI, dose reduction, and early stoppage all favored the exercise group, although they were not statistically significant.

Among the four studies that assessed treatment completion by receipt of full chemotherapy dose, three studies (75.0%) reported a significant benefit of exercise (63,83,85), including one with receipt of full chemotherapy dose as a primary outcome (85). In all four studies, the authors reported the percentage of individuals who received the full chemotherapy dose over the intended time frame without any dose reductions, dose delays, or early stoppage. In a pilot RCT by Allen *et al.* (63), people with locally advanced esophagogastric cancer were randomly assigned to 15 wk of supervised/home-based aerobic/resistance exercise (n = 26) or usual care (n = 28). Significantly more participants in the exercise group completed neoadjuvant

chemotherapy at full dose versus the control group (75.0% vs 46.4%, respectively; $P = 0.036$). Significantly fewer participants in the exercise group required a dose reduction or delay compared to the control group (16.0% vs 43.0%, respectively; $P = 0.041$). Similarly, Christodoulidis *et al.* (83) retrospectively compared people with stage I to IV esophagogastric cancer who underwent a 12 wk home-based multimodal neoadjuvant exercise program ($n = 47$) to participants who did not receive this program ($n = 45$). The program involved 150 min·wk^{-1} of moderate-intensity aerobic/resistance exercise, as well as telephone-based nutritional and psychological support. More participants in the intervention group completed neoadjuvant chemotherapy at full dose over 4 wk versus the control group (93.6% vs 77.7%, respectively; $P = 0.029$). Lastly, in a prospective single-arm study by Okada *et al.* (85), people with stage I to III pancreatic cancer underwent supervised aerobic and resistance exercise while in hospital for 1 to 2 wk after surgery. They were then discharged and returned to the hospital as outpatients during chemotherapy, where they received further supervised aerobic and resistance exercise. Treatment completion was specified as a primary outcome in this study. Compared to a historical control group, significantly more participants in the exercise group completed the full four courses of chemotherapy (93.0% vs 53.0%, respectively; $P < 0.001$).

Radiation Therapy

No completed studies on the effect of exercise on treatment completion in people undergoing radiation therapy were found, but two protocols were identified. Berntsen *et al.* (96) aim to report on the effect of exercise on the receipt of full dose collected from case records for people with breast, colorectal, and prostate cancer undergoing adjuvant radiation and radiation with curative intent without endocrine therapy. Grigoletto *et al.* (89) aim to investigate the effect of exercise on treatment completion via medical records in people with lung or head and neck cancers undergoing chemotherapy and/or radiation therapy.

Chemoradiation

Four studies in chemoradiation were identified (67–70); however, treatment completion was not a primary outcome for any of these studies. In a nonrandomized study by Dewberry *et al.* (69), people with esophageal cancer staged ≥IIb were allocated into usual care ($n = 11$) or a multimodal neoadjuvant program ($n = 11$) including exercise, nutrition, and psychological prehabilitation, depending on geographical proximity to the program location. The intervention program was 4 to 6 wk, depending on the chemoradiation schedule. No differences in chemotherapy dose reduction were found between the two groups (69). In a randomized study by Morielli *et al.* (68), people with stage II to IV rectal cancer were randomized to the exercise group ($n = 18$) or usual care ($n = 18$). The exercise intervention included 6 wk of supervised aerobic exercise training three times a week throughout chemoradiation, and then 6 wk of home-based physical activity after chemoradiation before surgery. There were no differences in radiation dose, or the number of participants who received >80% of their planned chemotherapy (68). Xu *et al.* (70) randomized people with esophageal cancer staged ≥IIb to supervised aerobic exercise classes three times a week for 4 to 5 wk ($n = 30$) or usual care ($n = 29$). No significant differences in chemotherapy dose reduction, chemotherapy treatment discontinuation, or radiation interruption breaks were reported (70).

Hormone Therapy

Three studies reported on the effect of exercise on hormone therapy treatment completion in people being treated for breast cancer (71–73); none of these three studies had treatment completion as the primary outcome. Irwin *et al.* (71) randomized participants with stage 0 to III breast cancer to usual care ($n = 60$) or a resistance and aerobic exercise program ($n = 61$) for 12 months. There were no differences in self-reported medication adherence to aromatase inhibitor therapy at 12 months, captured by daily logs (80.0% exercise compared to 76.0% usual care). Myers *et al.* (72) reported similar results in a single-arm pilot study ($n = 27$) of people with stage I to III breast cancer who were enrolled in a 6-wk virtual, group-based supervised resistance and aerobic exercise intervention. No difference in self-reported medication adherence was found using Voils' self-reported medication nonadherence measure (39) (25.0% who missed, skipped, or did not take medication over the past 7 d at baseline compared to 8.0% at end of intervention; $P = 0.13$). Tamaki *et al.* (73) conducted a 52-wk trial comparing home-based physical activity ($n = 102$) to usual care ($n = 37$) in people with breast cancer (stage not reported) and preliminary results reported a significant increase in self-reported medication adherence in the exercise group (99.0% vs 92.0%, $P = 0.03$) (Table 2).

Immunotherapy

No completed studies investigating the effect of exercise on treatment completion outcomes in people receiving immunotherapy were identified. One protocol was identified as potentially relevant. Mikkelsen *et al.* (95) aim to report on the impact of exercise on dose reductions and treatment discontinuation in people undergoing first-line chemotherapy, immunotherapy, or targeted therapy during treatment for advanced, unresectable pancreatic, biliary tract, or lung cancers.

Targeted Therapy

No completed studies investigating the effect of exercise on treatment completion in people receiving targeted therapy were identified. One study protocol by Mikkelsen *et al.* (95), as outlined for immunotherapy previously, includes targeted therapy completion as an outcome.

IMPLICATIONS AND FUTURE DIRECTIONS

As outlined in the EPiCC Framework, understanding the role of exercise in treatment completion is an important metric to justify the importance of including exercise as part of standard of care (66). There is a growing need in exercise oncology research to (i) evaluate the effect of exercise on treatment completion as a primary outcome, (ii) use standardized treatment completion outcomes with consistent definitions, and (iii) examine the effects of exercise on treatment completion within a specific treatment combination and sequence. This review focused on intrahabilitation. Given the few studies reporting significant results, perhaps this is not the main justification for the inclusion of exercise interventions during treatment, compared with the wealth of evidence to support improvements in physical function, quality of life, and other relevant outcomes. Or, the optimal timing for an exercise intervention may need to

be before treatment starts in order to improve future treatment tolerance. Future reviews should explore other combinations of treatment types and sequences as outlined in the EPiCC Framework.

The outcomes for treatment completion are best delineated in chemotherapy. However, further standardization of the definitions of outcomes is necessary. There is a wide variety of outcomes used in exercise oncology studies and even variable terms used for similar outcomes. There is a need to unify terminology and definitions across the exercise oncology field, and possibly in line with the outcomes used in drug and preclinical studies. The use of RDI as an outcome in exercise studies has greatly improved the quality of reporting. However, accurately calculating RDI is challenging. It should also be noted that, although the planned dose serves as the denominator for calculating RDI, oncologists may choose to reduce the planned dose of a chemotherapy schedule for certain patients, including those with poor performance status or for older adults, and the planned dose denominator may not be a guideline-concordant dose. Additionally, oral medications can be taken as a whole, half, or not taken, which may impact how precisely oral medication dose can be tailored and reduced. This may impact determination of potential change in dose intensity that can be observed. This in turn could impact sample size calculations, which should be considered for future studies.

Efforts from the ENICTO network to operationalize the approach to calculating RDI in the context of real cancer care is an important advance (19). There is a need for a similar effort for the other outcomes related to chemotherapy listed in Table 1. This is timely; our original review on treatment completion outcomes published in 2019 only identified eight randomized studies reporting on chemotherapy completion rate (50). There has been a large increase in the available literature to examine this question and more to come based on the number of protocols identified.

Specifically, the ENICTO network is carrying out four studies to determine whether exercise and medical nutrition interventions during chemotherapy have an impact on RDI through different mechanisms (19) (Table 4). The Adaptive Randomization of Aerobic Exercise during Chemotherapy in Colon Cancer (ACTION) study is expected to improve RDI via exercise-induced reductions in fat mass and preservation of lean mass, which will, in turn, improve the pharmacokinetic properties of chemotherapy. The Tele-Exercise during Chemotherapy Trial (TNT) is anticipated to improve RDI by exercise-induced reductions in systemic reactive oxygen species and improving hemoglobin and neutrophil recovery after every chemotherapy cycle in people with gastrointestinal cancer. The Trial of Exercise And Lifestyle (TEAL) intends to improve patient-reported chemotoxicities and RDI by minimizing the decrease in muscle mass caused by chemotherapy through aerobic and resistance exercise and medical nutrition in people with ovarian cancer. Finally, the TeleHealth Resistance Exercise Intervention to Preserve Dose Intensity and Vitality in Elder Breast Cancer Patients (THRIVE-65) hypothesizes that maintenance of muscle mass through resistance training and protein supplementation will lead to improved physical function and fewer patient-reported symptoms, thus, preventing the need for symptom-related chemotherapy dose reductions (19).

For future studies of exercise interventions in people undergoing radiation therapy, the authors suggest reporting on treatment completion outcomes, particularly RDI and interruptions to radiation therapy treatment, including unplanned dose delays as a result of treatment-related side effects or patient-related outcomes (*i.e.*, tolerance). The authors suggest considering radiation duration as part of the calculation of RDI (Fig. 3). Furthermore, the inclusion of outcomes such as receipt of full dose, dose reduction, and dose delay may provide a more fulsome picture when reporting on treatment completion. Like chemotherapy, these outcomes require a unified definition. Exercise studies during chemoradiation have often reported chemotherapy outcomes separate from radiation outcomes, which prevents the aggregation of data and any conclusions about the effect of exercise on chemoradiation as a whole. If outcomes are kept separated by treatment, then definitions from chemotherapy and radiation therapy literature should be referenced.

With immunotherapy, hormone therapy, and targeted therapy, an effort to align terminology and definitions with outcomes reported in drug trials is warranted. Specifically, given that many of these are provided as oral medications, standardizing the reporting of medication adherence is crucial. For a systematic review on adherence to oral therapies, readers are directed to Greer *et al.* (104), which also identifies methods for measuring medication adherence used in the literature. These primarily include patient self-report and pharmacy/insurance records, the latter of which specify if a patient's prescription has been filled/refilled. Trials are also incorporating pill diaries

TABLE 4. Description of ongoing ENICTO studies

Study	Cancer Type	Study Design, Arms, Intervention Length	Delivery Site	Outcome	Expected Sample Size	Exercise Prescription
ACTION—Adaptive Randomization of Aerobic Exercise During Chemotherapy in Colon Cancer	Colon	Bayesian, multistage, response adaptive 5 arms, length of chemo	Home, virtual monitoring	RDI	219	AeT: 3-6× a week, 20–60 min·d^{-1} 70% (±10%) age-predicted HR_{max}
TEAL—Trial of Exercise and Lifestyle in Women with Ovarian Cancer	Ovarian	Randomized 1:1 2-arms 18 wk	Clinic and home	RDI	200	AeT: 1–7× a week, 150 min·wk^{-1}, RPE 4–6/10 ReT: 2× a week, 2 × 10 reps
THRIVE-65—Tele-Health Resistance Exercise Intervention to Preserve Dose Intensity and Vitality in Elder Breast Cancer Patients	Breast (age ≥65 yr)	Randomized 1:1 2-arms length of chemo	Clinic-to-home, tele-health monitoring	RDI	270	AeT: 3–5× a week, 20–60 min·d^{-1} 55%–85% VO_{2peak}
TNT—Dose-Response of Aerobic Training during Chemotherapy for Colorectal Cancer	Gastrointestinal (locally advanced)	Randomized 1:1:1 3 arms ~32 wk	Home, remote real-time monitoring	RDI	216	AeT: 3× a week, 30 min·d^{-1}, low–mod ReT: 2× a week, 30–60 min, RPE 8/10

AeT, aerobic training; chemo, chemotherapy; HR_{max}, maximum heart rate; mod, moderate intensity; RDI, relative dose intensity; ReT, resistance training; RPE, rating of perceived exertion.
[Adapted from (18). Copyright © 2025 The authors CC-BY-NC. Used with permission.]

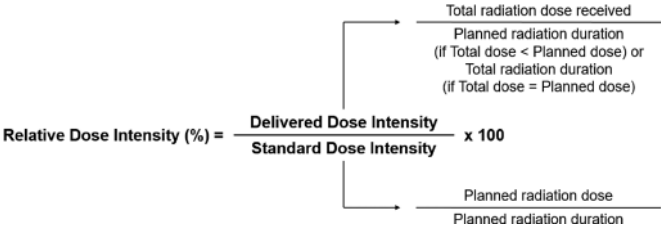

Figure 3. Relative dose intensity formula proposed for radiation therapy.

to monitor medication adherence. However, these current methods of measuring adherence to oral cancer therapies have potential limitations, such as self-report bias and not knowing if a patient actually took their medication in the case of pharmacy/insurance records. Advances in medication packaging may be an option to better quantify medication adherence. Example of options such as hidden sensors in pill bottle caps and blister packs have been used to improve patient adherence to medication (105). Although this methodology has not been widely used to date, it may be an avenue of future studies. Although adverse treatment side effects are a key reason for poor oral medication adherence, there are other factors to consider, such as financial cost, lack of social support in terms of poor physician-patient relationships or inadequate follow-up, and difficulties accessing health care providers to prescribe and manage the treatment (106).

Overall, oncologists often consider indicators of physical health, such as performance status, physical function, and the presence of comorbidities, in treatment-related decisions and subsequent dose modifications. This context suggests that any supportive care intervention that can mitigate declines in physical health, physical function, and manifestation of other comorbidities has the potential to support treatment completion. In the absence of definitive studies, the role of exercise as part of supportive care to manage symptoms of cancer treatments should be encouraged.

LIMITATIONS

A key challenge to examining the effect of exercise on treatment completion is identifying studies that report on treatment completion as an outcome using a standard search strategy. First, there are a variety of terms used for treatment completion outcomes, which make constructing search terms difficult. In the construction of our search strategy, keywords such as adhere* or tolera* made up the majority of the search. The only MeSH terms used to describe treatment completion were "Treatment Adherence and Compliance" and "Medication Adherence." The authors suggest that these terms are used to index future publications which examine treatment completion outcomes. Due to these limitations in the search, a number of reported studies were identified through systematically reviewing reference lists and gray literature repositories, or by recommendation from the expert writing team.

Second, a variety of different terms have been used to describe treatment completion, and — at times — different terms of what is operationally the same outcome. Although attempts to unify and propose definitions have been made in this review, there may be terms that have been grouped under unified outcomes that are not reflective of the original author's intent. Thus, this review and the included studies must be understood as a perspective for progress, rather than a systematic review and analysis.

Third, to date, treatment completion has not been a primary outcome for many studies. Out of the 30 published studies identified, only 3 studies specified treatment completion as a primary outcome (77,79,85), whereas only one protocol specified treatment completion as a primary outcome (97). As a result, the majority of studies have reported treatment completion as a secondary or exploratory outcome. Thus, many of the studies are not powered to provide significant insight into the effect of exercise on cancer treatment completion.

Fourth, 33% of the identified studies were conducted in early-stage breast cancer and focused on completion of chemotherapy that was delivered with curative intent. This is similar to the finding of a prior review from our team by Bland *et al.* (50). Although there seems to have been a greater representation of tumor types in this review, more research is needed to understand how exercise may impact treatment completion for individuals receiving treatment for other cancer types, and other types of treatment beyond curative intent chemotherapy (*i.e.*, potentially life-prolonging treatment, palliative treatment). Only one identified trial investigated exercise's effect on completion of palliative cancer treatment, namely, chemotherapy for people with metastatic colorectal cancer and multiple myeloma. More thorough investigations into the role of exercise as intrahabilitation for targeted and immunotherapy in the modern cancer care landscape are needed.

Fifth, adequately reported adherence to the exercise intervention was only captured in 50% of studies included in this review. Other studies either did not report adherence or only reported attendance (*i.e.*, number of sessions completed or proportion of sessions completed out of total prescribed). Attendance reflects the extent that individuals were present during the exercise prescription; it does not provide information about the degree to which participants adhered to the overall dose of exercise (*i.e.*, intensity, duration, volume for resistance exercise) (107). Without complete exercise adherence information, it is difficult to determine whether any reported lack of benefit of exercise on treatment completion is due to the exercise intervention not being effective, or an insufficient dose of exercise being completed by participants.

Lastly, the scope of this review is limited to the effect of exercise on treatment completion and is not able to comment on the relationship between exercise and treatment efficacy outcomes (*e.g.*, pathologic complete response, tumor size, risk of recurrence, and survival). Although it is established that higher treatment completion is associated with improved outcomes, there are no published clinical trials on the effect of exercise on the risk of recurrence or survival as a primary outcome. The effect of exercise after a cancer diagnosis on treatment efficacy from preclinical to observational data has been well reviewed (108,109) and has also been reported as a secondary outcome in follow-up reports of clinical exercise trials (62,110–112). There are a number of trials underway, including the CHALLENGE Trial looking at disease-free survival for people with stage II–III colon cancer who are randomized to a 3-yr physical activity behavior change intervention (113,114), and exciting results from recent studies looking at improved pathologic complete response in neoadjuvant breast cancer treatment (77).

SUMMARY

The delivery of full treatment dose intensity is considered a quality-of-care indicator in clinical oncology; the identification of new strategies to improve the ability of people being treated for cancer to better tolerate treatments and improve treatment completion should be a priority. Engaging in an exercise intervention before and/or during cancer treatment has the potential to allow individuals to be prescribed and tolerate more of the planned treatment dose, which may in turn improve treatment efficacy and survival. There is a growing body of literature on the potential of exercise to improve treatment completion, and emerging evidence to support the benefit of exercise on treatment tolerance. More research is needed to reach a conclusion on the effect of exercise on treatment completion in treatment modalities besides chemotherapy, and greater attention to tumor sites other than breast is encouraged. Unified terminology and definitions are presented in this review in an effort to streamline future research in this field. As the field of exercise oncology continues to grow and efforts are made to incorporate exercise into standard care, consistent terminology will allow for better communication within the field and with clinicians.

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