

# Resistance training interventions across the cancer control continuum: a systematic review of the implementation of resistance training principles

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## ABSTRACT

**Objectives** The primary purpose of this systematic review is to examine the extant resistance training (RT) cancer research to evaluate the proportion of RT interventions that: (1) implemented key RT training principles (specificity, progression, overload) and (2) explicitly reported relevant RT prescription components (frequency, intensity, sets, reps).

**Design** A qualitative systematic review was performed by two reviewers (CMF and PNH) who inspected the titles and abstracts to determine eligibility for this systematic review. Identified papers were obtained in full and further reviewed. Data were extracted to evaluate the application of principles of training, along with specific RT components.

**Data sources** Electronic databases (PubMed, EMBASE, CINAHL, Cochrane, PEDro, PsychInfo, Cancer Lit, Sport Discus, AMED, Cochrane Central Register of Controlled Trials) and reference lists of included articles from inception to May 2016.

**Results** 37 studies were included. The principle of *specificity* was used appropriately in all of the studies, *progression* in 65% and *overload* in 76% of the studies. The most common exercise prescription (~50%) implemented in the studies included in this review were 2–3 days/week, focusing on large muscle groups, 60–70% 1 repetition maximum (RM), 1–3 sets of 8–12 repetitions.

**Conclusions** Reporting of RT principles in an oncology setting varies greatly, with often vague or non-existent references to the principles of training and how the RT prescription was designed.

## INTRODUCTION

To date, the prevailing evidence in the field of exercise oncology supports the safety and efficacy of exercise as a means to attenuate many of the treatment-related adverse effects, such as risk for cardiovascular disease, increased fatigue and diminished physical functioning and quality of life.<sup>1–11</sup> Moreover, the culmination of the extant literature supporting the benefits of exercise for patients with cancer and cancer survivors has resulted in the release of several position stands and expert statements from numerous international agencies advocating physical activity in this population.<sup>12–15</sup> These recommendations provide beneficial guidance in developing safe and effective exercise programming for patients with cancer and cancer survivors. However, the exercise response in a patient population with cancer can vary based on the cancer type, treatment type, dose and duration,

and time along the cancer continuum. Consequently, it is plausible that applying a generic resistance training (RT) prescription to a heterogeneous patient population with cancer may unintentionally mask the full therapeutic potential of RT as a supportive care intervention in the treatment of cancer.<sup>16</sup>

The development and implementation of RT programmes are traditionally guided by key RT principles such as specificity (training stimulus must be specific to the desired outcome), progression (training stimulus must be systematically progressed to provide a greater than normal stress) and overload (greater than normal stress must occur for adaptation to occur).<sup>17–18</sup> Implementation of these training principles are used to systematically guide the manipulation of primary components of the RT stimulus including duration, load and volume. Consequently, given that the application of these training principles is integral to optimising the improvements accompanying RT observed across the cancer control continuum, determining the extent to which key scientific principles of RT (ie, specificity, progression and overload) (table 1) are implemented in RT interventions is an integral consideration for guiding future exercise prescription approaches designed for patients with cancer and cancer survivors.

There is a critical need for the scientific principles of RT and the components of the RT stimulus, to be applied rigorously and reported in detail in RT prescription to allow for appropriate evaluation of the feasibility, efficacy and effectiveness of RT interventions in a patient population with cancer. Careful attention to the implementation of these principles and reporting of RT stimulus components is important to accurately evaluate the therapeutic efficacy of RT as a supportive care intervention across the cancer control continuum.<sup>19–20</sup> Accordingly, a thorough evaluation of the individual components of the exercise prescription including frequency, intensity, time, sets and reps is also warranted.

Previous reviews have examined interventions with regard to their application of common principles of exercise training across various patient populations with cancer.<sup>19–20</sup> However, to the best of our knowledge, a comprehensive review focusing specifically on the application of RT principles and RT stimulus components/prescription has yet to be conducted. We contend that determining the extent to which RT principles have been implemented in interventions is an important objective given the present state of knowledge of RT prescription



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**Table 1** Exercise training principles and description of RT components

Principle and definition	Criteria for this review
Specificity: Training should be specific to muscles trained, and be relevant to desired outcomes	The intervention is designed to induce improvements in a primary outcome
Progression: The amount of load or resistance must be increased, providing a greater stress than the body is used to for continuous adaptation	The intervention gradually increased in frequency, sets, reps and/or load over the course of the intervention
Overload: Greater than normal stress must occur for fitness to improve	Interventions included baseline testing to determine exercise intensity (ie, 1 RM), or rationale that intervention was of sufficient intensity
Component of RT prescription	Description
Frequency	How many days per week
Intensity	Either per cent 1 RM, RPE or RM
Time	Duration of session
Sets	How many sets of each exercise were performed
Repetition range	What was the repetition range for each set
Exercise selection	An outline of the exercises used for the intervention

RM, repetition maximum; RPE, rate of perceived exertion; RT, resistance training.

in cancer care. Evaluating the extent to which key RT principles have been implemented is an important, yet presently understudied, aspect that may influence the utility of implementing RT in supportive care of cancer.

## OBJECTIVE

The primary purpose of this systematic review is to examine the extant RT–cancer research to evaluate the proportion of RT interventions that: (1) implemented key RT training principles (specificity, progression, overload) and (2) explicitly reported relevant RT prescription components (frequency, intensity, sets, reps, etc).

## METHODS

### Design

This was a qualitative systematic review. Before conducting searches of any kind, a priori eligibility criteria were established and applied to the search yield.

### Eligibility criteria for selecting studies

We assessed randomised controlled trials (RCTs) for eligibility for inclusion. To be included, RCTs must have examined a RT intervention in isolation, and included adult patients with cancer or cancer survivors who were actively undergoing cancer treatment or had cancer treatment with curative intent, and have been published in English in a peer-reviewed journal.

### Data sources

Scientific databases (PubMed, EMBASE, CINAHL, Cochrane, PEDro, PsychInfo, Cancer Lit, Sport Discus, AMED, Cochrane Central Register of Controlled Trials) were searched in February 2016. A subsequent search was performed in May 2016 to ensure inclusion of any additional articles that were published in the interim. Search terms related to cancer (cancer, oncology, tumour, malignancy, chemotherapy) and RT (weight training, RT, strength training) were entered in different combinations as

Medical Subject Heading terms and keywords where appropriate. All terms were applied to every database and the search strategy as applied to PubMed can be found in online supplementary appendix 1. Manual searches were also conducted using the reference lists of other narrative and meta-analytic review of the exercise oncology literature. CMF performed the initial search using the search terms in all possible combinations which was then confirmed by PNH.

### Article selection

Two authors (CMF and PNH) independently screened the title and abstract of every citation found in the literature search. Two lists were compared to achieve consensus for eligibility. Identified papers of relevance were then obtained in full and the eligibility criteria were applied independently by both authors. Any discrepancies were resolved by discussion and consensus with an independent reviewer (BCF). Consistent with PRISMA guidelines, the flow diagram in [figure 1](#) outlines the results of the computerised searches.

### Data extraction

Data extraction guidelines were developed to systematically extract data from each study under the following headings: the population studied, cancer treatment (if applicable), total sample size, outcomes of interest, exercise programme details such as frequency, intensity, set, reps, etc, and incorporation of training principles such as overload and progression.

Relevant details of each study included in the study were extracted and rated independently by both authors according to each principle of training. Any discrepancies were settled via discussion among all authors (CMF, PNH and BCF). Incorporation of principles was determined by a study having detail on their intervention that fell within the operational definition of each principle outlined in [table 1](#). Incorporation and/or reporting of the principle was assigned a ‘Y’, whereas ‘UC’ was assigned if it was unclear whether or not the principle was used, or if it was used but inconsistently applied (eg, an intervention progressed the load to a point, then discontinued progression). ‘NR’ was assigned if a principle was not reported in the intervention. Details if/how and the level to which principles of progression and overload were reported in each study were characterised by one of the following statements: (1) no mention of if/how principle was incorporated, (2) mentioned the principle, but no description of how it was incorporated, (3) brief, but vague description of incorporation of principle and (4) clear description of incorporation of principle. The reporting score for each principle is outlined in [table 2](#). Additionally, the specific details of each RT intervention have been outlined in supplementary appendix 2. Characteristics of each intervention according to the FITT principle, frequency (how often), intensity (prescribed intensity of the activity), time (duration of each bout) and type (excluded as all studies included were RT interventions), along with details on prescribed sets, repetition ranges and exercises were extracted. An overview of the exercise training principles and the description of RT components are provided in [table 1](#).

### Risk of bias

The Physiotherapy Evidence Database (PEDro) scale was used to assess the risk of bias in included studies. The PEDro scale rates internal study validity and the presence of statistical replicable information on a scale from 0 (high risk of bias) to 10 (low risk of bias) with  $\geq 6$  representing a cut-off score for studies with low risk of bias.<sup>21</sup>

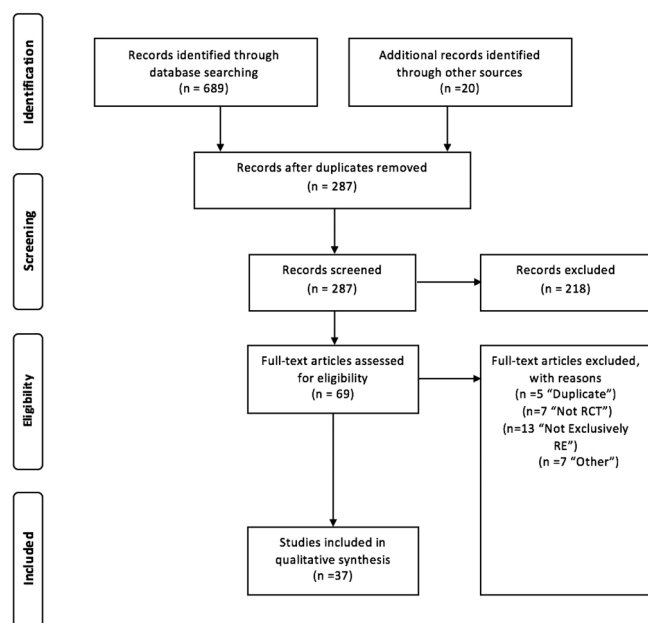


Figure 1 PRISMA flow diagram.

## Analyses

A summary of findings for each study was compiled to depict sample characteristics, number of participants, study duration and outcomes of interest (table 2). A summary of the application of key training principles, the RT stimulus components of sets, reps and intensity used, as well as an outline of the exercises in the RT intervention session, is compiled into table 2. The proportion of interventions that applied each RT principle and explicitly reported the RT stimulus components was transformed into percentages via proportion of studies using a principle relative to the total number of studies included in this review.

## RESULTS

### Study characteristics

An outline of the study design, participant and intervention characteristics are provided in table 3. A total of 709 records were identified by the literature search, 69 of which were selected for full-text review ( $\kappa=0.68$ ). PEDro scores from the included studies ranged from 5 to 9. Items that were fulfilled by the majority of studies were 'eligibility criteria' ( $n=41$ ), 'random allocation' ( $n=41$ ), 'no baseline difference' ( $n=38$ ), 'between-groups statistical outcome' ( $n=37$ ), and 'point measures of variability' ( $n=41$ ). Roughly half of the studies concealed allocation ( $n=23$ ), or used the intention to treat principle in their analysis ( $n=25$ ). A majority of the studies failed with blinding of subjects ( $n=0$ ) and assessors ( $n=15$ ). Individual PEDro scores for each study are presented in table 3. A total of 37 studies involving 3251 participants met the inclusion criteria of the review ( $\kappa=0.87$ ). A total of 18 studies were conducted during adjuvant treatment (chemotherapy and/or radiation), whereas 19 studies were conducted after the completion of treatment. The length of the interventions ranged from 9 weeks to 52 weeks. Few studies in the review targeted one outcome measure as their primary outcome, with many aiming to improve a variety of physiological and psychosocial outcomes. Thus, all of the studies' outcomes are included in outcomes of interest in table 3. Figure 1 outlines the results of the searches and full-text reviews. Following full-text review, 32 studies were excluded for the following reasons: duplicate ( $n=9$ ),<sup>22–30</sup> not RCT ( $n=6$ ),<sup>31–36</sup> not exclusively RT ( $n=10$ ),<sup>6, 37–45</sup> other ( $n=7$ ).<sup>46–52</sup>

## Application of RT principles

An overview of the application of RT principles is provided in table 4. The principle of *specificity* was used appropriately by all of the studies (100%) by matching the intervention to the study objective (body composition, strength, physical function, lymphoedema symptoms, etc). The principle of *progression* was applied appropriately in 24 of the 37 (65%) studies. The principle was unclear or incorrectly applied in the remaining 13 (35%) studies. The principle of *overload* was applied appropriately by 28 (76%) of the 37 studies. The application of this principle was unclear or non-existent in the remaining nine (24%) studies.

## Reporting of RT components

All studies (100%) included in this review reported the *frequency* of sessions. Frequency ranged from 1 to 4 sessions per week. All but one (98%) of the studies reported the *intensity* of the exercise prescription. The intensity was prescribed either using a percentage of 1 repetition maximum (RM), or a target RM for a given session (eg, 8–10 RM). The duration of the entire RT intervention was reported in all studies (100%). Additionally, the duration of each RT session was reported by 13 (40%) studies. All studies (100%) reported the number of sets performed during the intervention. Sets performed during a given session ranged from 1 to 4. All studies reported the repetitions range prescribed during the intervention. The reps prescribed ranged from 6 to 20. The most commonly reported prescription (~50%) included in the review was 2–3 days/week, 1–3 sets, 8–12 reps at 60–80% of 1 RM, focusing on machine-based exercises for muscles of the chest, back, shoulders, arms, buttock, hips, thighs and calves.

## DISCUSSION

The primary purposes of this systematic review were to examine the extant RT–cancer literature to evaluate the proportion of RT interventions that: (1) implemented key RT principles (specificity, progression, overload) and (2) explicitly reported relevant RT prescription components (frequency, intensity, sets, reps, etc). A total of 37 studies examining RT in patient populations with cancer were included in this review. The principles of *specificity*, *progression* and *overload* were incorporated in 100%, 65% and 76% of the studies, respectively. Thus, there is meaningful variability in the implementation of the key RT principles of progression and overload across RT trials among patients with cancer and cancer survivors. Additionally, the majority of studies explicitly reported the relevant RT prescription components. The most common exercise prescription (~50%) implemented in the studies included in this review were 2–3 days/week, focusing on large muscle groups, 60–70% 1 RM, 1–3 sets of 8–12 repetitions. Taken collectively, the findings of the present review have important implications for RT prescription approaches as well as the design and delivery of future RT interventions targeting patient populations with cancer.

## Incorporation of RT principles

The principle of *specificity* was incorporated by all of the studies included in the review. All of the trials appropriately matched the RT intervention to a desired outcome of muscular strength, physical function or lymphoedema status. This is consistent with prior reviews of the exercise oncology literature reporting that the principle of specificity was reported in all RT studies.<sup>19, 20</sup> The incorporation of this principle ensures the most appropriate mode of exercise is selected to optimise the

Table 2 Application of the principles of training

Author	Spec	Prog	Reporting of Prog	Over	Reporting of Over	Freq (d/wk)	Intensity (% 1 RM or RPE)	Time (min)	Sets	Reps	Exercise outline
Ahmed <sup>25</sup>	Y	Y	3	Y	3	2	8–10 RM	60	1–3	8–12	Machine-based exercises aimed at muscles of chest, back, shoulders, and arms, as well as the buttocks, hips, and thighs
Brown et al. <sup>53 54</sup>	Y	Y	4	Y	3	2	10 RM	90	3	10	Machine-based exercises aimed at major muscle groups
Cornie <sup>55</sup>	Y	Y	4	Y	4	2	75–85% HL; 55–65% LL	NR	1–4	6–10 or 15–20	Machine-based exercises aimed at major muscle groups
Dolan <sup>56</sup>	Y	UC	2	Y	4	3	60–70%	NR	2	8–12	Machine-based exercises aimed at major muscle groups
Hagstrom <sup>23 57</sup>	Y	Y	4	Y	4	3	8 RM	60	3	8–10	Machine-based exercises aimed at major muscle groups, transitioning to free-weight, compound exercises aimed at the same muscle groups
Alberga <sup>58</sup>	Y	Y	3	Y	3	3	60–70%	NR	1–4	8–12	Machine-based exercises aimed at major muscle groups
Capozzi <sup>59</sup>	Y	UC	2	Y	3	2d Sup, 2d home	8–10 RM	NR	2–3	8	Bodyweight/free-weight exercises aimed at major muscle groups
Christensen <sup>60 61</sup>	Y	Y	2	Y	3	3	10–15 RM	NR	3	10–15	Machine-based exercises aimed at major muscle groups
Courneya <sup>62</sup>	Y	Y	3	Y	3	3	60–70%	NR	2	8–12	Machine-based exercises aimed at major muscle groups
Musanti <sup>63</sup>	Y	UC	2	UC	1		3–5 RPE	NR	1–2	8–10	Resistance bands aimed at major muscle groups
Ohira <sup>27</sup>	Y	NR		UC	1	2		NR	1–3	8–10	Variable resistance machines and free weights for muscles of the chest, back, shoulders and arms, as well as the buttocks, hips and thighs
Schmidt <sup>64</sup>	Y	UC	2	Y	3	2	50%	NR	1	20	Machine-based/free-weight exercises aimed at major muscle groups
Schmidt <sup>65</sup>	Y	UC	2	UC	2	1	50%	NR	1	20	Machine-based/free-weight exercises aimed at major muscle groups
Schmidt <sup>5</sup>	Y	UC	2	Y	3	2	60–80%	60	3	8–12	Machine-based exercises aimed at major muscle groups
Schmitz <sup>22</sup>	Y	Y	4	UC	2	2	8–10 RM	60	1–3	8–12	Machine-based/free-weight exercises aimed at muscles of chest, back, shoulders and arms, as well as the buttocks, hips and thighs
Schmitz <sup>66 67</sup>	Y	Y	4	Y	3	2	8–10 RM	90	3	10	Machine-based exercises aimed at major muscle groups
Simonavice <sup>68</sup>	Y	Y	4	Y	4	2	60–80%	NR	2	8–12	Machine-based exercises aimed at major muscle groups
Speck <sup>69</sup>	Y	UC	2	UC	1	2	8–10 RM	45–60	3	10	Bodyweight/free-weight exercises aimed at major muscle groups
Twiss <sup>70</sup>	Y	Y	4	UC	1	2	No more than 20 lbs	30–45	2	8–12	Exercises with hand/foot weights aimed at upper and lower extremities
Yuen <sup>71</sup>	Y	Y	3	UC	1	2–3	8–12 RM	NR	1–2	8–12	Exercises aimed at major muscle groups
Winters-stone <sup>9 72 73</sup>	Y	Y	4	Y	4	2d Sup, 1d home	60–70%	45–60	1–3	8–12	Bodyweight/free-weight exercises aimed at major muscle groups
Winters-stone <sup>26</sup>	Y	Y	4	Y	4	2d Sup, 1d home	8–15 RM	30–60	2–3	8–15	Machine-based exercises aimed at major muscle groups
Winters-stone <sup>74</sup>	Y	Y	4	Y	3	2	8–10 RM	45–60	3	10	Machine-based exercises aimed at major muscle groups
Steindorf <sup>75</sup>	Y	UC	2	Y	3	2	60–80%	60	3	8–12	Machine-based exercises aimed at major muscle groups
Jensen <sup>76</sup>	Y	UC	2	Y	3	2	60–80%	45	2–3	15–25	Large muscle groups, including the legs, arms, back and knees
Lombro <sup>77</sup>	Y	Y	3	Y	3	2–3	8–15 RM	NR	2–3	8–15	Machine-based exercises aimed at major muscle groups
Lombro <sup>78</sup>	Y	Y	3	Y	3	2–3	8–15 RM	NR	2–3	8–15	Machine-based exercises aimed at major muscle groups
Nilsen <sup>29</sup>	Y	Y	3	Y	4	3	10 RM, 6 RM, 90% of 10 RM	NR	1–3	6–10	Machine-based exercises aimed at major muscle groups
Nilsen <sup>28</sup>	Y	UC	2	Y	4	3	10 RM, 6 RM, 90% of 10 RM	NR	1–3	6–10	Machine-based exercises aimed at major muscle groups
Norris <sup>30</sup>	Y	Y	4	Y	4	2 or 3	60–70% to 80%	NR	2–3	8–12	Machine-based exercises aimed at major muscle groups
Santa Mina <sup>79</sup>	Y	Y	3	UC	2	3–5	12–15 RPE	30–60	2–3	8–12	Resistant bands aimed at major muscle groups

Continued



Table 2 Continued

Author	Spec	Prog	Reporting of Prog	Over	Reporting of Over	Freq (d/wk)	Intensity (% 1 RM or RPE)	Time (min)	Sets	Reps	Exercise outline
Segal <sup>80</sup>	Y	Y	3	Y	3	3	60–70%	NR	2	8–12	Machine-based exercises aimed at major muscle groups
Segal <sup>24</sup>	Y	Y	3	Y	3	3	60–70%	NR	2	8–12	Machine-based exercises aimed at major muscle groups
Winters-stone <sup>81</sup>	Y	Y	3	Y	3	2	8–15 RM	NR	1–3	8–15	Bodyweight/free-weight/machine-based exercises aimed at major muscle groups
Winters-stone <sup>74 82 83</sup>	Y	Y	4	Y	4	2d Sup, 1d home	60–70%	30–60	1–3	8–12	Bodyweight/free-weight exercises aimed at major muscle groups
Litterini <sup>84</sup>	Y	UC	2	Y	3	2	NR	NR	1	8–15	Machine-based exercises aimed at major muscle groups

d, day; NR, not reported; Over, overload; Prog, progression; RM, repetition maximum; RPE, rate of perceived exertion; Spec, specificity; Sup, supervised; UC, Unclear; Y, yes.

desired outcome. Furthermore, incorporating the specificity principle facilitates the likelihood that improvements in the outcomes of interest are attributable to the effects of the RT intervention.

The principle of *overload* was not incorporated in 24% of the interventions included in this review. The principle of *overload* states that a muscle must act against greater than normal resistance to ensure appropriate stimulation and adaptation. Most commonly in RT, overload can be expressed a percentage of 1 RM, or a RM range (ie, 8–12 reps). Failure to ensure that exercise provides an adequate stimulus to the muscle can lead to minimal, if any, improvements in the desired outcome. Overload was not incorporated by studies either failing to conduct a baseline assessment of strength to determine an initial training stressor, or providing an initial load that could be deemed insufficient relative to current standards. For example, a study included in this review began participants with no weight or 1-pound weights for their initial weeks.<sup>74</sup> While this can be appreciated as a safe approach to loading, it can also be interpreted as an overly conservative, potentially ineffective loading protocol that may undermine the extent to which the RT intervention will produce meaningful improvements in clinically relevant outcomes. A higher initial loading may have led to even greater improvements in the desired outcomes. Thus, while the load prescribed in many of the interventions may have been effective, the results should be interpreted with the consideration that optimal loading stimulus may not have been implemented in at least 24% of the trials.

The principle of *progression* was *insufficiently reported* in 35% of the interventions included in the review. These studies provided either very little, or no detail at all on if or how the RT programme was progressed across the intervention. While these studies included detail on the initial RT prescription characteristics, no information was available for how the training was progressed thereafter. For example, Ohira *et al*<sup>27</sup> did not specifically describe any progression of the RT stimulus across a 24-week intervention, whereas Schmidt *et al*<sup>64</sup> included the description of ‘any increase in intensity was based on the Borg scale’ as their specific reference to progression that was implemented during the RT intervention. The principle of progression is critical in the design of an exercise programme to ensure continued development. The body can quickly adapt to a given exercise stress; thus, to see continued improvements in a desired outcome, the training stimulus must be gradually increased. Previous reviews have found the principle of *progression* to be reported more often in RT interventions than in aerobic exercise interventions.<sup>19 20</sup> It is possible that inadequate implementation of the progression principle could minimise the effect of the RT intervention leading to misinterpretation of null findings as evidence of a lack of efficacy of the intervention rather than a non-optimal design of the load and volume comprising the RT stimulus. Consequently, the reporting of the principle of progression is critical for appropriate evaluation and replication of the RT intervention.

An exercise stimulus serves to create biological stress, disrupting cellular and systemic environments.<sup>85–88</sup> This disruption results in a multisystem biological stress response, whereby the body adapts to the stress in an attempt to withstand future perturbations.<sup>85–88</sup> Indeed, strategically dosed, chronic RT can result in an array of physiological adaptations and improvements in relevant clinical and patient-reported outcomes. However, the exercise stimuli must be sufficient to stress the system, yet balanced with the recognition that excessive stress can disrupt homeostasis to a point where maladaptation occurs, increasing

**Table 3** Study characteristics

Author	Cancer Type	Patient or Survivor Population	Treatment types	N	Duration of intervention (weeks)	Outcomes of Interest	Effects on Outcomes	PEDro score
Ahmed <sup>25</sup>	Breast	Survivor		45	24	Lymphedema symptoms, Strength	↑ strength, ↔ lymphedema symptoms	7
Brown et al <sup>53 54</sup>	Breast	Survivor		243	52	ASMM, strength	↔ ASMM, ↑ strength,	9
Cornie <sup>55</sup>	Breast	Survivor		62	12	Swelling, symptom severity, QOL, depression, strength, end, ROM	n/a	9
Dolan <sup>56</sup>	Breast	Patient	Chemo	242	Duration of Chemo	HB, CRF	n/a	8
Hagstrom <sup>23 57</sup>	Breast	Survivor		39	16	QOL, Fatigue, Muscle Strength, Inflammatory Markers, BC	↑ Inflammatory markers, strength, Fatigue, QOL	7
Courneya <sup>62</sup>	Breast	Patient	Chemo	242	Duration of Chemo	Muscle Strength, QOL, fatigue, depression, CRF	n/a	5
Musani <sup>63</sup>	Breast	Survivor		33	12	AC, strength, BC, ROM, fatigue, depression	↑ fatigue, depression	6
Ohira <sup>27</sup>	Breast	Survivor		86	24	Weight, strength, QOL, depression	n/a	8
Schmidt <sup>64</sup>	Breast	Patient	Chemo	67	12	Muscle Strength, AC, QOL, cog function	↑ Strength, QOL, cog function, ↔ fatigue, ↓ AC	9
Schmidt <sup>65</sup>	Breast	Survivor		33	24	BMI, QOL, fatigue, Submax endurance	↔ BMI, submax endurance ↑ QOL, fatigue	5
Schmidt <sup>5</sup>	Breast	Patient	Chemo	95	12	Fatigue, Depression, Cog Function	↔ fatigue, depression, cog function	5
Schmitz <sup>22</sup>	Breast	Survivor		78	12	BC, Insulin, ILGF	↑ BC, ↔ Insulin, ILGF	9
Schmitz <sup>66 67</sup>	Breast	Survivor		134	52	Incident BRCL, Muscle Strength, BC	↑ Incident BRCL, strength	6
Simonavice <sup>68</sup>	Breast	Survivor		27	24	BC, Bone Turnover, strength	↔ BC, Bone Turnover, ↑ strength	6
Speck <sup>69</sup>	Breast	Survivor		234	52	BIRS, QOL, Muscle Strength	n/a	8
Steindorf <sup>75</sup>	Breast	Patient	Chemo	155	12	Fatigue, QOL, Depression, Muscle strength, AC	↑ Fatigue, QOL, ↔ Depression	7
Twiss <sup>70</sup>	Breast	Survivor		223	104	Strength, balance	↑ strength, balance	8
Yuen <sup>71</sup>	Breast	Survivor		22	12	Fatigue, aerobic capacity	↑ aerobic capacity, ↔ fatigue, ↔ CRF	7
Winters-stone <sup>9 72 73</sup>	Breast	Survivor		106	52	BMD, BC, Strength, Physical function	↑ BC, strength, ↔ BMD, physical function	5
Winters-stone <sup>74</sup>	Breast	Survivor		258	52	BMD	↔ BMD	9
Winters-stone <sup>26</sup>	Breast	Survivor		71	52	BC, BMD, Bone Turnover	BC, BMD (hip)	5
Christensen <sup>60 61</sup>	Germ Cell	Patient	Chemo	86	9	QOL, BC, Muscle Strength, inflammatory markers	↑ QOL, BC & Muscle Strength: n/a, ↓ inflammatory markers	8
Jensen <sup>76</sup>	Gastrointestinal	Survivor		26	12	BC, Muscle Strength, FP	↑ BC, Muscle Strength, FP	5
Capozzi <sup>59</sup>	Head and Neck	Survivor		55	12	Aerobic Fitness, Upper/lower body strength, body composition	↑ Upper body strength, ↔ aerobic fitness, body composition, lower body strength	7
Lonbro <sup>78</sup>	Head and Neck	Survivor		41	24	Strength, BC, physical function	↑ BC, strength, physical function	5
Alberga <sup>58</sup>	Prostate	Patient	Radiation/ADT	121	24	Strength, BC, AC,	n/a	8
Nilsen <sup>29</sup>	Prostate	Patient	ADT	58	16	BC, Physical Function, QOL	↑ Physical function, ↔ QOL, BC	7
Nilsen <sup>28</sup>	Prostate	Patient	Radiation/ADT	23	16	CSA, myonuclei, satellite cells, strength	↑ CSA, strength, ↔ myonuclei, strength	6
Norris <sup>30</sup>	Prostate	Patient		30	12	Strength, Physical function, QOL, fatigue	n/a	8
Santa Mina <sup>79</sup>	Prostate	Patient	ADT	26	24	Adiponectin, leptin, IGF-1, aerobic capacity, anthropometrics, grip strength	↓ IGF-1 ↔ Adiponectin, leptin, aerobic capacity, anthropometrics, grip strength	5

Continued

Table 3 Continued

Author	Cancer Type	Patient or Survivor Population	Treatment types	N	Duration of intervention (weeks)	Outcomes of Interest	Effects on Outcomes	PEDro score
Segal <sup>80</sup>	Prostate	Patient	Radiation/ Chemo	121	24	QOL, CRF, BC, Muscular Strength, T, PSA, Hb	↑ Strength, Hb→QOL, CRF, BC, T, PSA	8
Segal <sup>24</sup>	Prostate	Patient	ADT	155	12	Fatigue, QOL, BC, Muscular Fitness	↑ Fatigue, QOL, Muscular Fitness, →BC	8
Winters-stone <sup>81</sup>	Prostate	Patient	None currently	64	24	BC, Muscle Strength	↑ Muscle Strength, →BC	8
Winters-stone <sup>82, 83</sup>	Prostate	Patient	ADT	51	52	BC, Insulin, IGF-1, Muscle Strength, Disability, SPPB, Pain, Fatigue	↑ BC, Muscle strength, Disability, Insulin, IGF 1	7
Litterini <sup>84</sup>	Mixed	Patient	Chemo/CT	52	10		↑ SPPB, Fatigue, →pain	5

the fatigue and the risk of injury.<sup>87 89 90</sup> The detailed reporting of progression and overload used in the exercise prescription process is an integral consideration in the design and delivery of RT interventions.

Vague descriptions of the exercise stimulus and application of progression can lead to misinterpretation and delivery in clinical or community settings. This can result in an inefficient exercise prescription, along with the potential for injury due to over-training or misapplication of a training stimulus. Moreover, the incorporation and reporting of these training principles are critical to avoid inaccurate conclusions about a negative trial outcome that may be more attributable to the intervention design than a lack of efficacy.

RT prescription is a complex art, involving the manipulation of numerous variables. Thus, explicit description of the exercise intervention is imperative to the evaluation and replication of studies.<sup>91–93</sup> In a recent systematic review of 73 systematic reviews, Slade and Keating<sup>94</sup> reported that the majority of reviews were unable to appropriately describe the exercise interventions included because the required information was poorly described or not described at all. In an attempt to rectify this, a standardised method for reporting exercise programmes was developed by Slade *et al*,<sup>91</sup> comprehensively detailing critical components of an intervention such as the location, level of supervision, detailed description of exercises, dose and progression, individualisation and instructor qualification/experience. Certainly, the inclusion of an exercise reporting grid would dramatically improve the ability to accurately evaluate, replicate and implement interventions. We recommend a standardised exercise-reporting tool, such as the one outlined by Slade *et al*,<sup>91</sup> to be considered by researchers and journals to enhance the quality of exercise reporting in oncology trials.

### RT prescription characteristics

In addition to evaluating the implementation of RT principles, determining the proportion of RT interventions that explicitly reported the relevant RT prescription components was also a primary objective of this systematic review. The present findings revealed that the majority of studies explicitly reported the relevant RT prescription components. Although the initial RT stimulus components were consistently reported in appropriate detail in virtually all the trials, details of if or how the initial RT stimulus components were modified across the trial were not consistently addressed. Specifically, the extent to which RT components such as load or volume were modified during the intervention to promote progression or overload were not described in detail. As noted previously, this is a primary contributing factor to the inability to determine if the principles of progression and overload were incorporated and not reported, or whether they were not incorporated at all.

It should be noted that the most common exercise prescription (~50%) implemented in the studies included in this review were based on the American College of Sports Medicine (ACSM) recommendations for RT. The ACSM guidelines recommend 2–3 days/week of RE, focusing on large muscle groups, 60–70% 1 RM, 1–3 sets of 8–12 repetitions.<sup>12–15</sup> Of the 33 studies included in this review, 18 used these guidelines, focusing on stimulating the whole body during each session. Given the benefits accompanying RT in trials implementing the ACSM recommendations, these guidelines appear to be effective at improving clinically relevant patient-reported outcomes including muscular strength, quality of life, fatigue, etc.

Nonetheless, it is also important to recognise there is considerable variability in the response and adaptation to a specific

training stimulus in an apparently healthy population.<sup>95</sup> Thus, it is possible the heterogeneity in the response to a given training stimulus may be compounded in an individual with cancer as a function of multiple aspects including, but not limited to, their present status in the cancer control continuum (pretreatment, during treatment or post-treatment), cancer site, treatment (type, dose, duration), age, comorbidities, activity level and body composition. For example, the exercise prescription for a patient with breast cancer undergoing chemotherapy will require modification to account for range of motion limitations of the upper body as a result of a port inserted for chemotherapy infusion, or surgery to remove a tumour. This may differ from a patient with lung cancer having radiation to the chest wall and is recovering from partial lung lobectomy. Indeed, a prostate cancer survivor on chronic androgen deprivation therapy will require a unique prescription to account for castrate levels of anabolic hormones. Additionally, any single RT prescription is unlikely to represent the optimal stimulus for all patients or yield a uniform magnitude of improvement across all outcomes relevant for treatment of patients with cancer. Accordingly, while there will be variability in the implementation and responses to RT in different patient populations with cancer across the cancer control continuum, there will also be heterogeneity in the responses to RT within patients of the same cancer type and/or diagnosis. Accordingly, RT prescriptions that personalise the intervention stimulus to the individual needs, preferences and tolerances are critical to the efficacy of integrating RT in the supportive care efforts. This emphasises the highly individualised nature of exercise prescription in an oncology setting, and the need to investigate different doses, frequencies, duration or load of RT.

The current national guidelines on physical activity in a patient population with cancer highlight the progress that the field of exercise oncology has made since the first published research 30 years ago. However, despite the advances in research and increased international recognition of the importance of integrating exercise in oncology treatment, the findings of the present review demonstrate the inconsistency with which fundamental principles of RT have been implemented in randomised controlled RT trials during and following cancer treatment. Accordingly, the findings suggest current approaches to RT prescription can be characterised as basic and potentially even underdeveloped.<sup>16</sup>

Conversely, several studies included in this review warrant attention for their novel design and exercise prescription approach. Hagstrom *et al* (2015) employed the traditional ACSM guidelines in breast cancer survivors (with 2 days a week of machine-based exercises: leg extension, machine bench press, back extension) for the first 8 weeks of the study. Participants then transitioned to free weight, barbell compound exercises (squat, deadlift, bench press, etc) for the second 8 weeks.<sup>23</sup> It is understood that free weight exercises stimulate muscle tissue to a greater degree than machine-based exercises.<sup>96–97</sup> Thus, Hagstrom's transition to free weight exercises represents an attempt to progress the exercise prescription and stimulate muscle tissue to a greater degree. Indeed, participants who participated in the RT intervention increased leg press strength by 40 kg in 16 weeks. When compared with a 20 kg increase in leg press strength in another study that used the ACSM guidelines for a year,<sup>66</sup> these findings highlight the critical importance of integrating progressive overload in the design and delivery of RT interventions and also underscore how the strategic manipulation of training variables can optimise the effects of RT in producing meaningful improvements in clinically relevant outcomes in patients with cancer and cancer survivors.

Nilsen *et al* used an undulating (more frequent variations in intensity) model of RT in patients with prostate cancer, alternating between a 10 RM, 6 RM and 80–90% 10 RM on day 1, 2 and 3 of their programme, respectively. Participants in the RT group exhibited improvements in muscle strength and cross-sectional area (CSA) following 16 weeks of the intervention. Unfortunately, the lack of a comparison intervention group using a more traditional approach to RT prescription precludes the opportunity to evaluate the comparative efficacy of the two RT approaches. There is substantial evidence supporting higher intensity exercise at eliciting greater muscle morphological and neuromuscular changes, along with strength, which ultimately facilitate greater improvements in functional mobility and quality of life.<sup>98–99</sup> Thus, the usage of an undulating RT model, with higher intensity exercise is a novel, progressive one in the exercise oncology field that warrants further investigation.

Norris *et al* examined the effects of RT frequency on strength, physical function and psychosocial outcomes in patients with prostate cancer. The researchers compared 12 weeks of different RT training frequency (2 days/week vs 3 days/week). The addition of the extra training session resulted in ~50% extra training volume. Potentially meaningful effects were found for lower body strength and select physical function outcomes in the 3-day/week group.<sup>30</sup> While the addition of an extra day of RT, with ~50% additional training volume shows initial promise, It is unclear if greater differences between training frequency and volume would emerge after a longer intervention period.

These recent studies signify a novel area of the field of exercise oncology, where there is more interest in the design of the RT interventions, with the aim to determine the extent to which systematic, strategic manipulation of dose, sequencing and progression of RT can optimise improvements in clinically relevant outcomes during and following cancer treatment.

### Practical application

Several position stands and roundtables have provided initial guidelines for implementing RT in a patient population with cancer with site-specific precautions.<sup>12–15</sup> Indeed, detailed guidelines of RT prescription among different cancer types, at different treatment time points, is beyond the scope of this review. However, we have outlined a few brief guidelines below:

- ▶ A comprehensive fitness evaluation is strongly recommended prior to beginning a RT programme to identify potential physical/psychosocial limitations to exercise. For example, a patient with prostate cancer may have difficulty in the seated position in the weeks following surgery, whereas a patient with breast cancer may need alterations in upper body exercise prescription to account for range of motion difficulty following surgery.
- ▶ A minimum of 2 days/week of RT is recommended for most patient populations, with the aim of maintaining/improving lean body mass throughout and following treatment. A total body approach of 6–8 exercises per session aimed at stimulating large muscle groups (leg press, leg curl, leg extension, Romanian deadlift, chest press, shoulder press, lat pulldown, seated row) is advocated.
- ▶ The incorporation and reporting of key RT principles is absolutely critical to the *continued* improvement in clinically relevant outcomes. Progression and overload should be incorporated on an individual basis according to patient response.
- ▶ Future studies should seek to investigate exercise prescription characteristics outside those proposed by ACSM, or compare these to traditional guidelines in an attempt to determine if an optimal dose–response relationship exists between exercise and target outcomes.



- ▶ A standardised exercise-reporting tool can be incorporated into future interventions to improve the ability to appropriately evaluate and replicate interventions.

Future studies grounded in scientific RT principles, examining different RT interventions, for longer duration, with transparency in reporting of the stimulus components of the RT intervention will ensure continued progress in the field. This, combined with current knowledge, can serve to advance the field and ensure correct interpretation and application of the intervention in a clinical and community setting.

### Limitations

Although we believe the present findings have meaningful implications for future RT interventions among patient populations with cancer, there are several limitations that should be acknowledged. First, the primary purpose of this review was to evaluate the extent to which RT principles were implemented in RT trials, not to explore if implementation of these principles influenced the effect of the RT interventions on relevant clinical or patient-reported outcomes. We contend that addressing the proportion of trials that implement RT principles and explicitly report the RT stimulus components is a critical initial step in advancing the knowledge of and application of RT across the cancer control continuum. Nonetheless, we recognise the importance of determining if implementation of RT principles impacts the benefits for patient populations with cancer. As more RCTs implementing the RT principles among patients with cancer and cancer survivors emerge, future reviews using standardised meta-analytic procedures to examine the influence of implementing these training principles on relevant outcomes are warranted.

The majority of studies included in this review were conducted in breast and prostate cancer. Thus, the paucity of studies conducted in patient populations with other types of cancer limit the generalisability of our review across the cancer control continuum. As studies investigating exercise in less common forms of cancer slowly emerge, the recommendations for RT can be expanded to a broader range of populations.

### SUMMARY/CONCLUSIONS

Results of the present review suggest there is meaningful variability in the implementation of the key RT principles of progression and overload across RT trials among patients with cancer and cancer survivors. Additionally, whereas the majority of studies explicitly reported the relevant initial RT prescription components, the extent to which RT components such as load or volume were modified during the intervention to promote progression or overload were not described in detail. Additionally, the majority of studies used RT prescription characteristics that fell within ACSM's guidelines.<sup>15</sup>

### What are the findings?

- ▶ The majority of studies apply a largely generic resistance training (RT) prescription to a considerably heterogeneous population.
- ▶ More recently, studies have begun to investigate different doses, frequencies, timing and progression of RT in the patient population with cancer.
- ▶ There is a critical need for RT interventions to rigorously apply the principles of RT, along with clear reporting of intervention characteristics.

### How might it impact on clinical practice in the future?

- ▶ Practitioners are encouraged to use central tenets of RT prescription when designing and implementing programmes in a patient population with cancer, with special attention being paid to principles of progression and overload.
- ▶ These findings may encourage practitioners to experiment with different doses, frequencies and progression of RT to provide an optimal training stimulus in the patient population with cancer.
- ▶ While the safety and efficacy of RT has been demonstrated during and after cancer in a variety of patient populations with cancer, there has been considerably less research conducted in less common cancers (ie, germ cell, head and neck). Accordingly, practitioners should err on the side of caution with RT prescription and may need to progress at a slower rate according to patient response.

**Correction notice** This article has been corrected since it was published Online First. Table 3 has been replaced with a new version.

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