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The development of an evidence-based physical self-management rehabilitation programme for cancer survivors

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g University for Applied Sciences, Hanze University Groningen, Groningen, the Netherlands

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Abstract

Objective: This paper describes the development of a physical training programme for cancer patients. Four related but conceptually and empirically distinct physical problems are described: decreased aerobic capacity, decreased muscle strength, fatigue and impaired role physical functioning. The study aimed to identify the optimal content for an exercise programme that addresses these four physical problems, based on the highest level of evidence available. The study further aimed to review the evidence available on the delivery of the programmes. The final goal was to develop a programme in which content and delivery are based on the best available evidence.

Methods: Literature searches (PUBMED and MEDLINE, to July 2006) on content looked for evidence about the efficacy of exercise on aerobic capacity, muscle strength, fatigue and impaired role physical functioning. Literature searches on delivery looked for self-management and/or self-efficacy enhancing techniques in relation to outcome, adherence to and/or adoption of a physically active lifestyle.

Results: Evidence on the effectiveness of exercise in cancer patients varies and increases when moving from muscle strength (RCT level), fatigue and physical role functioning to aerobic capacity (all at the meta-analysis level). Effect sizes for aerobic capacity were moderate, while effect sizes for fatigue and physical role functioning were zero and/or small. Many of the studies have significant methodological shortcomings. There was some evidence (meta-analyses) that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the quality of life in cancer patients, and on exercise adherence and later exercise behaviour.

Conclusion: Limited data are available on the effectiveness of exercise for cancer patients. Although evidence supports the positive effects of exercise on exercise capacity during and after completion of cancer treatment, the effects for fatigue and role functioning are ambiguous. Evidence on the effectiveness of progressive exercise training on muscle strength is promising. In addition, some evidence supports the positive effects of self-management programmes and self-efficacy enhancing programmes on health outcomes, exercise adherence and later exercise behaviour.

Practice Implications: The resulting programme was developed on the basis of the highest quality of evidence available regarding content and delivery. The content is based on information obtained from the present review, and on the recommendations of the American College of Sports Medicine. Potential advantages of the programme include: (a) tailored physical training towards focusing on the patient’s established problems and (b) delivery of the training as a self-management programme that might have beneficial effects on health outcome, exercise adherence and a long-term physically active lifestyle.

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Keywords: Cancer; Exercise; Fatigue; Self-management; Rehabilitation
1. Introduction

Due to improvements in diagnostics and treatment regimes, the survival rate of cancer patients is increasing. As a result, cancer is now considered to be a chronic disease and the attention paid to the quality of life (QoL) of patients after cancer treatment is increasing. Approximately 30% of all survivors report a decreased QoL due to physical and psychosocial problems following cancer and consequent treatment, and indicate that they need professional support [1] such as rehabilitation.

Physical training seems to be essential in the rehabilitation of cancer survivors. This is the case because, firstly, psychosocial interventions are less likely to improve physical and functional problems [2]. Secondly, physical training is reported to improve QoL beyond the benefits of psychotherapy [3]. Thirdly, improvement in physical functioning following a rehabilitation programme is associated with a simultaneous decrease in fatigue [4]. Lastly, very recent studies reveal that increased physical activity after a cancer diagnosis reduces the risk of cancer recurrence and mortality [5,6].

Physical training should be aimed at reducing long-term physical problems. Physical side effects that occur during cancer treatment, such as anaemia, pain, nausea, vomiting and sleep disorders, may affect daily functioning and QoL during that phase. Other physical and functional problems persist over time, including a decreased oxygen uptake, reduced muscle strength, fatigue and limited physical role functioning, and these continue to affect cancer patients’ QoL. Physical exercise has the potential to overcome such long-lasting problems [4,7,8].

These four problems, which are further discussed in Box 1, are to some extent interrelated, but appear to be empirically different. For example, aerobic capacity seems to be no different in Hodgkin’s disease patients with or without chronic fatigue and it is therefore thought that aerobic capacity does not play a major role in fatigue [7,8]. However, whether fatigue is a cause or a consequence of these factors is still unknown [36].

Box 1. The most important and long-lasting physical problems in cancer patients.

A decreased maximal oxygen uptake ($V_{\text{O}_2\text{max}} < 20\text{ ml/kg min}$) is reported in about 13–30% of survivors after Hodgkin’s disease [25,26] and non-Hodgkin’s disease patients [26]. The physical performance of 70% of patients with solid tumours and haematological cancers is classified as ‘poor’ (50–54% of reference $V_{\text{O}_2\text{max}}$) or ‘very poor’ (50% of reference $V_{\text{O}_2\text{max}}$) [27]. A decreased oxygen uptake or aerobic capacity may reflect the difficulty the cardio-respiratory system has in delivering oxygen throughout the body and/or problems of the musculoskeletal system in extracting oxygen from the blood during aerobic exercise. Both radiotherapy and chemotherapy appear to have negative side effects on the cardio-respiratory system [7,28] and on the musculoskeletal system [23].

Significant muscle wasting and consequent decreased muscle strength [29] affects about 50% of persons with cancer [4,23,30,31]. Although the exact mechanisms are unclear, it is generally accepted that cancer-induced muscle wasting is a multifactorial process that is mediated by factors such as reduced energy intake, proinflammatory cytokines [9,31], accelerated muscle protein degradation [23,32] and bed rest.

About 61–99% of cancer patients experience fatigue during and following cancer treatment [33–35]. Cancer-related fatigue, which is multidimensional in nature [36], might be caused by cancer-induced anaemia and tumour necrosis, but is also attributed to a reduced activity pattern as a consequence of prescribed bed rest [33,34]. Fatigue is associated with psychosocial problems such as anxiety and depression [37,38], reduced self-efficacy [39], sleep disorders, distress [33] and difficulty coping [31]. However, whether fatigue is a cause or a consequence of these factors is still unknown [36].
Many cancer patients report reduced physical and reduced role functioning due to physical problems [35]. Physical performance limitations, e.g. climbing stairs, walking short and long distances [40], were found to be significantly more prevalent among recent (54%) and long-term (53%) cancer survivors when compared to subjects with no cancer history (21%) [41]. Limitations in role functioning due to physical problems, such as reduced participation in social and sport activities [32,35], are reported in about 30% of both short and long-term cancer survivors, compared to 13% of subjects with no cancer history [41].

role in the pathophysiology of fatigue [9]. Therefore, aerobic capacity and fatigue would require different physical training modalities. Although physical training programmes are commonly reported to be effective in improving aerobic exercise capacity and muscle strength, and in reducing fatigue and ameliorating physical role functioning [2,10,11], to date it is still unclear what type of exercise is most optimal in addressing each of the four defined problems. The optimal intervention modality, intensity, timing and duration are still unknown, despite the fact that there is growing evidence for the positive effects of physical training [12,13]. Standardized guidelines about the specific interventions are currently available for healthy individuals [14] but lacking for cancer patients. Until now, various programmes consisting of aerobic training, muscle strength training and/or flexibility training have been described for cancer patients, all with varying content [15].

In addition to the content, the efficacy of a physical training programme may depend on the delivery. However, no information is available concerning the best way to deliver a training programme for cancer patients. In that regard, a patient-oriented intervention, characterized by active participation, taking personal responsibility and changing lifestyle [16,17]. Patient-oriented interventions such as self-management may include monitoring and managing symptoms, adherence to treatment regimes, maintaining a healthy lifestyle and managing the impact of the illness on daily functioning [17]. Self-management generally consists of six processes: goal selection, information collection through monitoring, information processing and evaluation (in relation to norms), decision-making, action and self-reflection [18]. In self-management, self-efficacy – which is a patient’s own belief in his or her ability to perform specific actions or change specific thinking patterns and, thus, manage and minimize the symptoms – is believed to be of primary importance [16,19]. Self-management may have more beneficial effects than traditional interventions.

Self-management programmes may also be relevant to exercise adherence and for the adoption of a physically active lifestyle after the completion of a physical training programme [20]. A good level of adherence to an exercise regime may be a prerequisite for the effectiveness of exercise because a certain combination of duration, intensity and frequency per week is needed to improve aerobic fitness [14]. Prior studies reveal that adherence to and compliance with physical training programmes ranges from 52 to 89% [21], and underline the need to promote adherence to physical training regimes. It is important that patients adopt a physically active lifestyle after the prescribed training programme because low activity levels, which appear to be common in cancer patients [22], are associated with morbidity and mortality. Low level physical activity might also be considered as a maintaining cause for several of the physical problems discussed above, which means that low activity levels may induce a vicious circle of reduced oxygen capacity, lower muscle strength and more fatigue [23]. To improve exercise adherence and encourage the adoption of a physically active lifestyle, a structured exercise programme combined with theory-based behavioural interventions has been recommended [21]. Therefore, theoretical frameworks such as self-management [18] based on the self-regulation of behaviour [24], and self-efficacy stimulating techniques [19] based on social cognitive theory, may be relevant to exercise adherence and adoption, in addition to traditional physical training.

The aim of the present article is to describe the development of an exercise intervention that is designed to improve the four most relevant cancer-related physical problems (Box 1). Firstly, the literature will be reviewed for evidence regarding the content (such as modality and intensity) of the programme for each defined problem, and secondly for the evidence available regarding the issue concerning delivery discussed above. Lastly, a programme will be presented in which content and delivery are based on the best available evidence.

2. Methods

Our first aim was to review the evidence regarding the content of programmes that address the four physical problems mentioned in Box 1, based on the highest level of evidence available. A computerized search in PUBMED and MEDLINE (to July 2006) was conducted using the Mesh terms ‘cancer’, ‘aerobic’ and ‘exercise capacity’. Additional searches were conducted using ‘cancer’, and ‘muscle strength’ and/or ‘resistance training’, and ‘cancer’ ‘exercise’ and ‘fatigue’. ‘Physical role functioning’ is not a Mesh term but this broad term includes physical abilities that range from simple mobility to the engagement in complex activities that require adaptation to an environment. Thus, it includes objective and perceived mobility and participation in daily activities, which are important QoL domains. Therefore, a search was conducted with ‘cancer’, ‘exercise’ and ‘quality of life’ and only the relevant physical domains were taken into account. All searches were limited to ‘meta-analyses/systematic review’ and ‘English language’. When no meta-analyses/systematic reviews were found, the same Mesh terms were used and combined with ‘Randomized Controlled Trials’(RCTs). When no RCTs were
<table>
<thead>
<tr>
<th>Study</th>
<th>During/after treatment</th>
<th>Type of cancer</th>
<th>Type of exercise programme</th>
<th>Intensity (load)</th>
<th>Frequency, volume, duration</th>
<th>Number of patients</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burnham [48]</td>
<td>After surgery, radiation</td>
<td>Breast and colon cancer</td>
<td>Low intensity aerobic exercise Moderate-high intensity exercise Treadmill and cycling</td>
<td>25–40% HRR 40–60% HRR</td>
<td>3/week 14–32 min 10 weeks</td>
<td>21</td>
<td>No differences between low and high intensity Combined groups showed significant increase in $V_{\text{O}2\text{max}}$ in EG (18.6%) compared to CG (2.7%)</td>
</tr>
<tr>
<td>Courneya [49]</td>
<td>After surgery, receiving adjuvant therapy</td>
<td>Colorectal</td>
<td>Home-based aerobic exercise Walking and cycling</td>
<td>50–75% MHR</td>
<td>3–5/week 10–30 min 16 weeks</td>
<td>102</td>
<td>No differences between groups with respect to cardiovascular fitness</td>
</tr>
<tr>
<td>Courneya [50]</td>
<td>After surgery, radiation and chemotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling</td>
<td>70–75% $V_{\text{O}2\text{max}}$</td>
<td>3/week 15–35 min 15 weeks</td>
<td>53</td>
<td>14.5% increase in $V_{\text{O}2\text{max}}$ in EG and a decrease (~3%) in (W)CG</td>
</tr>
<tr>
<td>Dimeo [7]</td>
<td>During chemotherapy and autologous PBSCT</td>
<td>Mixed solid tumours</td>
<td>Supervised aerobic exercise Cycling on bed ergometer</td>
<td>50% HRR (220-age-resthr)</td>
<td>Daily 15–30 min during hospitalisation</td>
<td>70</td>
<td>Loss of maximal performance was 27% higher in CG compared to EG EG had significantly higher scores on maximal performance compared to CG, data NA</td>
</tr>
<tr>
<td>Dimeo [51]</td>
<td>After chemotherapy and autologous PBSCT</td>
<td>Mixed solid tumours and non-Hodgkin’s</td>
<td>Supervised interval-endurance exercise Treadmill walking</td>
<td>80% MHR (calculated)</td>
<td>5 week 3–30 min 6 weeks</td>
<td>32</td>
<td>Increase in maximal performance (speed) in EG (34%) was significantly higher compared to control (21%)</td>
</tr>
<tr>
<td>Dimeo [52]</td>
<td>After surgery</td>
<td>Lung and gastrointestinal cancer</td>
<td>Aerobic exercise group versus relaxation group</td>
<td>80% MHR/ Borg 13–14</td>
<td>5/week 15–30 min 3 weeks</td>
<td>69</td>
<td>EG showed 8% increase in maximal performance, no change in RG</td>
</tr>
<tr>
<td>Study (year)</td>
<td>Intervention Details</td>
<td>Type of Exercise</td>
<td>VO2max (%) Increase</td>
<td>Week(s)</td>
<td>Notes</td>
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<tr>
<td>Herrero [53]</td>
<td>After surgery and radiotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise</td>
<td>70–80% MHR Weight that allowed 12–15 repetitions, then adjusted to 8–10 repetitions, followed by an increase of 5–10%</td>
<td>3/week 70 min (20–30 min aerobic) 11 exercises 8–15 repetitions, 3 sets 8 weeks</td>
<td>EG showed an increase in VO2max (9%) and a decrease in CG (−6%)</td>
<td></td>
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<tr>
<td>Kim [54]</td>
<td>During chemotherapy or radiotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling, walking, running</td>
<td>60–70% VO2 max</td>
<td>3/week 30 min 8 weeks</td>
<td>EG showed significant increase in VO2max (8%), no significant changes in CG (2%)</td>
<td></td>
</tr>
<tr>
<td>MacVicar [55]</td>
<td>During chemotherapy</td>
<td>Breast</td>
<td>Supervised aerobic interval exercise; alternating higher and lower intensity Cycling</td>
<td>60–85% HRR</td>
<td>3/week, 20–30 min 10 weeks</td>
<td>VO2max and maximum workload improved in EG (40%) compared to placebo (stretching exercises) and to CG</td>
<td></td>
</tr>
<tr>
<td>Nieman [56]</td>
<td>After surgery, chemotherapy or radiotherapy</td>
<td>Breast</td>
<td>Supervised cardiovascular exercise Walking</td>
<td>75% MHR Weight unspecified</td>
<td>3/week 30 min, 7 different exercises 12 repetitions 8 weeks</td>
<td>Modest improvement in aerobic capacity EG; walking distance increased significantly in EG compared to CG, heart rate tended to be reduced, data NA</td>
<td></td>
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<tr>
<td>Segal [57]</td>
<td>During radiotherapy, chemotherapy and hormonal therapy</td>
<td>Breast</td>
<td>Cardiovascular exercise self-directed Walking Versus supervised programme and usual care</td>
<td>50–60% VO2max</td>
<td>5/week self-directed group 3/week supervised group, 2 days at home No specification of volume 26 weeks</td>
<td>VO2max in CG, and increased 3.5% in self-directed group and 2.5% in supervised group (N.S) Supervised exercise showed significantly more increase in VO2 compared to usual care and to self-directed group only in patients not receiving chemotherapy</td>
<td></td>
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<tr>
<td>Thorsen [58]</td>
<td>After chemotherapy</td>
<td>Mixed cancer diagnosis</td>
<td>Supervised home-based aerobic programme Walking and cycling</td>
<td>Borg on 13–15 60–70% MHR</td>
<td>Minimal 2/week, more were allowed At least 30 min 14 weeks</td>
<td>VO2 max in EG, and 10% in CG</td>
<td></td>
</tr>
</tbody>
</table>
found, the same Mesh terms were used and combined with ‘Clinical Trials’. Because we were interested in the specific effects of exercise, studies that focused only on exercise were included. Physical interventions combined with other interventions (such as diet or psychotherapy) were excluded because of potential interaction effects. Controlled studies identified from meta-analyses that focused on the problems discussed above were taken into account. Furthermore, additional searches were performed to include controlled studies that were published after the RCTs included in the meta-analyses. If no studies of cancer patients were available, we searched for studies of other patient groups with chronic illness. We reviewed the evidence and screened the quality of the RCTs on methodological criteria such as randomization procedure, description of interventions, relevance of outcome measures, adverse events, withdrawal/dropout, sample size, and intention-to-treat analysis [42]. Furthermore, we analysed the content of the various programmes. If pre-intervention and post-intervention data were reported, we computed changes which were expressed as percentages of change from the baseline.

Our second aim was to review the evidence available on the delivery of the programme. A search in PUBMED and MEDLINE (to July 2006) was conducted using the following terms related to delivery: ‘self-management and/or self-efficacy’ and ‘adherence and/or physically active lifestyle’, all combined with ‘exercise and cancer’. All searches were limited to ‘meta-analyses/systematic review’ and ‘English language’. When no meta-analyses were found, additional searches were performed with the same terms combined with ‘Randomized Controlled Trials’ and ‘Clinical Trials’. If no studies were available for cancer patients, supplementary searches were performed using the same terms combined with other patient populations and/or the general population.

For the actual programme we applied principles of intervention mapping [43], which is a process for developing theory and evidence-based health education programmes, including (1) creating a matrix of proximal programme objectives, (2) selecting theory-based intervention methods and practical strategies, and (3) designing and organizing a programme.

3. Results

3.1. Evidence concerning the content

Four meta-analyses [12,44–46] and two systematic reviews [13,47] on the effect of exercise and aerobic capacity, fatigue and QoL in cancer patients were found. The meta-analyses and systematic reviews and additional controlled studies published after the meta-analyses revealed 12 relevant studies on exercise capacity [7,48–58], 14 on fatigue [48,50,52,58–68] and 19 on physical QoL [48–50,53,54,57–59,61–71]. Many studies reported on more than one outcome measure. Therefore, there is some overlap between the studies. No meta-analyses or systematic reviews were found but nine randomized controlled studies reported on the effect of exercise training on muscle strength [53,56,67,69,70,72–75]. The controlled studies found are presented in Tables 1–4.

<table>
<thead>
<tr>
<th>Study</th>
<th>During/after treatment</th>
<th>Type of cancer</th>
<th>Type of exercise programme</th>
<th>Type of exercise</th>
<th>Frequency, intensity, duration</th>
<th>Number of patients</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coleman [72]</td>
<td>During chemotherapy and stem cell transplantation</td>
<td>Multiple myeloma</td>
<td>Home-based aerobic exercise</td>
<td>Walking</td>
<td>12–15 Borg</td>
<td>3/week 24</td>
<td>Significant increase in lean body mass in EG compared to CG.</td>
</tr>
<tr>
<td>Hayes [69]</td>
<td>After chemotherapy and HSCT</td>
<td>Mixed cancer diagnoses</td>
<td>Aerobic exercise and strength training</td>
<td>Cycling and walking</td>
<td>70–90% MHR</td>
<td>3/week 12</td>
<td>Significant effect of group and time for leg press and sit-stand test, but not for bench press.</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Body Area</td>
<td>Exercise Type</td>
<td>MHR</td>
<td>Frequency</td>
<td>Duration</td>
<td>Outcome</td>
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</tr>
<tr>
<td>Nieman [56]</td>
<td>After surgery chemotherapy radiotherapy</td>
<td>Breast</td>
<td>Supervised cardiovascular exercise Walking Weight training</td>
<td>75% MHR</td>
<td>3/week</td>
<td>8 weeks</td>
<td>Leg extension strength tended to increase more in EG compared to CG, N.S., data NA</td>
</tr>
<tr>
<td>Mello [73]</td>
<td>After bone marrow transplant</td>
<td>CML, AML, NHL, MDS</td>
<td>Interval aerobic exercise Walking Active range of motion exercises/muscle stretching</td>
<td>70% MHR</td>
<td>Daily</td>
<td>6 weeks</td>
<td>EG showed higher values for all muscle groups compared to CG Exercise group increased for 3 of 8 (UE) and 5 of 10 muscle groups (LE), data NA</td>
</tr>
<tr>
<td>Ohira [70]</td>
<td>After radiotherapy surgery chemotherapy</td>
<td>Breast</td>
<td>Supervised weight training followed by self-directed weight training Comparison EG with delayed group</td>
<td>Resistance machines and free weights not specified</td>
<td>2/week</td>
<td>26 weeks</td>
<td>Changes in bench press were 63% in EG versus 12% in delayed group Leg press 1-RM increases were 38% versus 9% for delayed group</td>
</tr>
<tr>
<td>Schmitz [74]</td>
<td>After radiation, chemotherapy</td>
<td>Breast</td>
<td>Supervised weight training followed by self-directed with training, comparison with waitlist controls</td>
<td>No weight for upper extremity Weight for lower extremity based on the ability to lift 8–10 times</td>
<td>2/week</td>
<td>6 months supervised, 6 months maintenance WLC from months 7 to 12</td>
<td>Significant increase in lean muscle mass (2.3%) compared to controls (no change)</td>
</tr>
<tr>
<td>Segal [67]</td>
<td>During hormone therapy</td>
<td>Prostate</td>
<td>Supervised resistance exercise</td>
<td>60–70% of 1-RM increase of 0.5 lb when &gt;12 repetitions were completed</td>
<td>3/week</td>
<td>12 weeks</td>
<td>EG showed higher levels of upper (40%) and lower body (32%) muscular fitness compared to WCG (~8% and ~4%, respectively)</td>
</tr>
<tr>
<td>Winningham [75]</td>
<td>During adjuvant chemotherapy</td>
<td>Breast</td>
<td>Supervised cycle interval protocol</td>
<td>60–85% VO2 max</td>
<td>3/week, 20–30 min</td>
<td>10 weeks</td>
<td>Increase of lean mass in EG compared to controls, data NA</td>
</tr>
<tr>
<td>Study</td>
<td>During/after treatment</td>
<td>Type of cancer</td>
<td>Type of exercise programme</td>
<td>Intensity (load)</td>
<td>Frequency, volume, duration</td>
<td>Number of patients</td>
<td>Outcome</td>
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<tr>
<td>Burnham [48]</td>
<td>After surgery, radiation, surgery</td>
<td>Mixed</td>
<td>Low intensity aerobic exercise Moderate-high intensity exercise Treadmill and cycling</td>
<td>25–40% HRR 40–60% HRR</td>
<td>3/week 14–32 min 10 weeks</td>
<td>21</td>
<td>Fatigue decreased in EG but not differing significantly from CG</td>
</tr>
<tr>
<td>Campbell [59]</td>
<td>During adjuvant chemotherapy/radiotherapy/combined</td>
<td>Breast</td>
<td>Supervised aerobic training Walking and cycling Muscle strengthening exercises</td>
<td>60–70% MHR (age adjusted) Muscle strengthening not specified</td>
<td>2/week 10–20 min 12 weeks</td>
<td>22</td>
<td>No significant differences in fatigue between EG and CG</td>
</tr>
<tr>
<td>Courneya [50]</td>
<td>After surgery, radiation, chemotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling</td>
<td>70–75% VO2max</td>
<td>3/week 15–35 min 15 weeks</td>
<td>53</td>
<td>Significant reduction in fatigue in EG (53%) compared to CG (19%)</td>
</tr>
<tr>
<td>Dimeo [60]</td>
<td>During chemotherapy</td>
<td>Mixed solid tumours, haematological</td>
<td>Supervised aerobic exercise Biking on a bed ergometer</td>
<td>50% HRR interval Mean workload 30 (±5) Watt</td>
<td>Daily 15 to 30 min with rest of 1 min Unspecified duration</td>
<td>63</td>
<td>Fatigue in EG remained unchanged and increased (25%) in CG during hospitalisation</td>
</tr>
<tr>
<td>Dimeo [52]</td>
<td>After surgery</td>
<td>Lung and gastrointestinal</td>
<td>Aerobic exercise group Versus relaxation</td>
<td>80% MHR/ Borg 13–14</td>
<td>5/week, 15–30 min 3 weeks</td>
<td>69</td>
<td>Fatigue improved in both groups (21 versus 19%), N.S.</td>
</tr>
<tr>
<td>Headley [61]</td>
<td>During chemotherapy</td>
<td>Breast</td>
<td>Home-based stretching and repeated flexion and extension exercises, video instruction</td>
<td>No resistance</td>
<td>3/week 30 min 2 weeks</td>
<td>32</td>
<td>EG showed significantly less increase in fatigue (FACT-F) than CG, data NA</td>
</tr>
<tr>
<td>Houborg [62]</td>
<td>After surgery</td>
<td>Colorectal</td>
<td>Supervised mobilisation exercises Aerobic training Strength training Continuation at home EG compared to placebo</td>
<td>Not specified Not specified Weight at 50–80% of 1-RM</td>
<td>6/week 45 min during hospitalisation (≈ 10 days) and after discharge at home: ≈ 11 weeks</td>
<td>119</td>
<td>No significant differences in fatigue between groups, data NA</td>
</tr>
<tr>
<td>Mock [63]</td>
<td>During radiation</td>
<td>Breast</td>
<td>Home-based progressive brisk programme Walking</td>
<td>Self-paced</td>
<td>4–5/week 20–30 min 6 weeks</td>
<td>46</td>
<td>Fatigue decreased in EG and increased in CG, significant, data NA</td>
</tr>
<tr>
<td>Mock [64]</td>
<td>During radiotherapy, chemotherapy</td>
<td>Breast</td>
<td>Home-based exercise Walking</td>
<td>Self-paced</td>
<td>5–6 week 15–30 min 6 weeks to 6 months during cancer treatment</td>
<td>52</td>
<td>Fatigue decreased significantly more in HW (i.e. patients who walked &gt; 90 min per week) (−14%) compared to LW (increase of 37%)</td>
</tr>
<tr>
<td>Author</td>
<td>Intervention</td>
<td>Disease</td>
<td>Type of Exercise</td>
<td>Intensity</td>
<td>Frequency</td>
<td>Duration</td>
<td>Fatigue Improvement</td>
</tr>
<tr>
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</tr>
<tr>
<td>Mock [65]</td>
<td>During radiotherapy, chemotherapy</td>
<td>Breast</td>
<td>Home-based exercise, brisk walking</td>
<td>50–70% MHR</td>
<td>5–6 /week</td>
<td>6 weeks</td>
<td>No differences in fatigue between EG and CG due to dilution of treatment. Fatigue increased significantly more in non-compliers than in full compliers and more in low walkers (77%) than in high walkers (20%).</td>
</tr>
<tr>
<td>Pinto [66]</td>
<td>After radiation, surgery and chemotherapy</td>
<td>Breast</td>
<td>Home-based exercise, walking, biking, swimming, counseling and pedometers</td>
<td>55–65% MHR</td>
<td>2–5/week</td>
<td>10–30 min</td>
<td>More reduction in fatigue in EG (36%) compared to controls (1.4%).</td>
</tr>
<tr>
<td>Segal [67]</td>
<td>During hormone therapy</td>
<td>Prostate</td>
<td>Supervised resistance exercise</td>
<td>60–70% of 1-RM, increase of 0.5 lb when &gt;12 repetitions were completed</td>
<td>3/week</td>
<td>8–12 repetitions, 9 exercises</td>
<td>EG showed improvement in fatigue during daily living activities (2%) compared to WCG that showed a decline in fatigue (−5%).</td>
</tr>
<tr>
<td>Thorsen [58]</td>
<td>After chemotherapy</td>
<td>Mixed cancer diagnosis</td>
<td>Supervised home-based aerobic programme, walking and cycling</td>
<td>Borg on 13–15/20</td>
<td>Minimal 2/week, more allowed</td>
<td>At least 30 min</td>
<td>Fatigue decreased more in CG (40%) compared to EG (15%).</td>
</tr>
<tr>
<td>Windsor [68]</td>
<td>During radiotherapy</td>
<td>Prostate</td>
<td>Home-based aerobic exercise, walking</td>
<td>60–70% MHR</td>
<td>3/week</td>
<td>30 min</td>
<td>Fatigue (BFI) increased in CG and ≈ in EG during RT, data NA</td>
</tr>
<tr>
<td>Study</td>
<td>During/after treatment</td>
<td>Type of cancer</td>
<td>Type of exercise programme</td>
<td>Intensity (load)</td>
<td>Frequency, volume, duration</td>
<td>Number of patients</td>
<td>Outcome Provided</td>
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<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Burnham [48]</td>
<td>After surgery, radiation, surgery</td>
<td>Mixed</td>
<td>Low intensity aerobic exercise Moderate-high intensity exercise treadmill Cycling</td>
<td>25–40% HRR 40–60% HRR</td>
<td>3/week 14–32 min 10 weeks</td>
<td>21</td>
<td>Combined exercise groups showed significant increase in QoL (9.4%) in EG compared to CG (−1.9%) Energy measure improved significantly in EG (−16%) compared to control (3.5%)</td>
</tr>
<tr>
<td>Campbell [59]</td>
<td>During adjuvant chemotherapy, radiotherapy, combined</td>
<td>Breast</td>
<td>Supervised aerobic training Walking and cycling Muscle-strengthening exercises</td>
<td>60–70% MHR (age adjusted) Muscle strengthening not specified</td>
<td>2/week 10–20 min 12 weeks</td>
<td>22</td>
<td>EG showed significantly more improvement than CG in walking distance (32% versus −5%) and in physical activity (103% versus 1.2%) and in QOL (17% versus −4%).</td>
</tr>
<tr>
<td>Courneya [49]</td>
<td>After surgery, receiving adjuvant therapy</td>
<td>Colorectal</td>
<td>Home-based aerobic exercise Walking and cycling.</td>
<td>50–75% MHR</td>
<td>3–5/week 10–30 min 16 weeks</td>
<td>102</td>
<td>No differences between groups. Patients who improved in fitness showed more improvement (4%) on FACT-C than decreased fitness group (−2%)</td>
</tr>
<tr>
<td>Courneya [50]</td>
<td>After surgery, radiation, chemotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling</td>
<td>70–75% $V_{O2\text{max}}$</td>
<td>3/week 15–35 min 15 weeks</td>
<td>53</td>
<td>Increase in physical wellbeing in EG (8%) compared to (W)CG (−8%)</td>
</tr>
<tr>
<td>Hayes [69]</td>
<td>After chemotherapy and PBSCT</td>
<td>Mixed lymphatic cancer diagnoses</td>
<td>Aerobic exercise treadmill walking and cycling Resistance training</td>
<td>70–90% MHR Weight set to induce failure between 8 and 20 repetitions</td>
<td>3/week 20/40 min 3 months</td>
<td>12</td>
<td>Physical QoL improved (20%) in EG and not in CG</td>
</tr>
<tr>
<td>Headley [61]</td>
<td>During chemotherapy</td>
<td>Stretching and repeated flexion and extension exercises</td>
<td>No resistance</td>
<td>No resistance</td>
<td>3/week 30 min 12 weeks</td>
<td>32</td>
<td>EG showed significantly less decline in physical wellbeing compared to CG during CT; data NA</td>
</tr>
<tr>
<td>Herrero [53]</td>
<td>After surgery and radiotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling on ergometer Resistance training</td>
<td>70–80% MHR Weight that allowed 12–15 repetitions, than adjusted to 8–10 repetitions, followed by an increase of 5–10%</td>
<td>3/week 70 min (20–30 min aerobic) 11 exercises 15 repetitions 8 weeks 3 sets</td>
<td>16</td>
<td>EG showed an increase in physical function (7%) and no change in CG</td>
</tr>
<tr>
<td>Reference</td>
<td>Stage</td>
<td>Tumor Type</td>
<td>Intervention</td>
<td>Description</td>
<td>Frequency</td>
<td>Duration</td>
<td>Outcome Note</td>
</tr>
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</tr>
<tr>
<td>Houborg [62]</td>
<td>After surgery</td>
<td>Colorectal</td>
<td>Supervised mobilisation exercises aerobic training Strength training Continuation at home</td>
<td>EG compared to placebo Not specified Not specified Weight at 50–80% of 1-RM</td>
<td>6/week Not specified</td>
<td>45 min during hospitalisation (≈ 10 days) and after discharge at home: ≈ 11 weeks</td>
<td>All indices of physical function decreased postoperative day seven and returned to preoperative level 90 days post operatively, with no significant differences between groups, data NA</td>
</tr>
<tr>
<td>Kim [54]</td>
<td>During chemotherapy or radiotherapy</td>
<td>Breast</td>
<td>Supervised aerobic exercise Cycling, walking, running</td>
<td></td>
<td>3/week</td>
<td>60–70% VO2 max 30 min 8 weeks</td>
<td>No between group changes Significant increase in EG compared to CG in voluntary exercise (31% versus 4%) and in energy expenditure (31 versus 4%) and a decrease in sedentary activity (−12% versus −6%)</td>
</tr>
<tr>
<td>Mock [63]</td>
<td>During radiation</td>
<td>Breast</td>
<td>Home-based progressive Brisk walking</td>
<td>Self-paced</td>
<td>4–5/week</td>
<td>20–30 min 6 weeks</td>
<td>EG showed significantly higher scores on 12 min WD (4%) compared to CG (−5%)</td>
</tr>
<tr>
<td>Mock [64]</td>
<td>During radiotherapy, chemotherapy</td>
<td>Breast</td>
<td>Home-based exercise Walking</td>
<td>Self-paced</td>
<td>5–6 week 15–30 min 6 weeks to 6 months during cancer treatment</td>
<td>HW (i.e. patients who walked &gt; 90 min per week) showed significantly higher scores than LW on functional ability (12 min WD: 6% versus −0.3%) and on self-reported physical activity (39% versus −38%) than LW. Physical functioning decreased significantly more in LW (45%) compared to HW (16%)</td>
<td></td>
</tr>
<tr>
<td>Mock [65]</td>
<td>During radiotherapy or chemotherapy</td>
<td>Breast</td>
<td>Home-based aerobic exercise Brisk walking</td>
<td>50–70% MHR</td>
<td>5–6 /week 15–30 min 6 weeks</td>
<td>EG showed significantly higher scores on WD than CG, but no differences in physical functioning (data NA) were found. HE showed higher scores than LE on walking distance (6% versus −0.2%), on physical functioning (5% versus −8%) and on activity levels (34% versus −14%)</td>
<td></td>
</tr>
<tr>
<td>Ohira [70]</td>
<td>After radiotherapy surgery chemotherapy</td>
<td>Breast cancer</td>
<td>Supervised weight training Followed by own weight training Resistance machines and free weights not specified</td>
<td></td>
<td>2/week</td>
<td>9 exercises 26 weeks</td>
<td>Physical global score improved by 2.1% in EG compared with a worsening by 1.2% in CG</td>
</tr>
<tr>
<td>Study</td>
<td>During/after treatment</td>
<td>Type of cancer</td>
<td>Type of exercise programme</td>
<td>Intensity (load)</td>
<td>Frequency, volume, duration</td>
<td>Number of patients</td>
<td>Outcome</td>
</tr>
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</tr>
<tr>
<td>Pinto [71]</td>
<td>After surgery, radiotherapy, chemotherapy over the past 3 years</td>
<td>Breast (sedentary)</td>
<td>Supervised aerobic exercise / Treadmill walking, cycling / Strength training</td>
<td>60–70% MHR</td>
<td>3/week 30 min 12 weeks</td>
<td>24</td>
<td>EG showed 8% reduction in heart rate at 75W, controls were not measured. Changes in self-reported condition were higher (31%) in EG than in CG (−19%)</td>
</tr>
<tr>
<td>Pinto [66]</td>
<td>After radiation, surgery and chemotherapy</td>
<td>Breast</td>
<td>Home-based cardiovascular exercise / Walking, biking, swimming, counselling and pedometers</td>
<td>55–65% MHR</td>
<td>2–5/week 10–30 min 12 weeks</td>
<td>68</td>
<td>EG reported higher scores than CG on walking speed (6% versus 1%), on physical activity level (142% versus 6%) and on energy expenditure (7% versus 0.5%)</td>
</tr>
<tr>
<td>Segal [57]</td>
<td>During radiotherapy, chemotherapy hormonal therapy</td>
<td>Breast</td>
<td>Cardiovascular self-directed programme / Walking / Versus supervised programme and usual care</td>
<td>50–60% VO$<em>2</em>{max}$</td>
<td>5/week self-directed group 3/week supervised group 2 days at home no specification of duration 26 weeks</td>
<td>123</td>
<td>Increase in physical functioning in self-directed group (7.5%) and in supervised group (3.5%) and a decrease in usual care</td>
</tr>
<tr>
<td>Segal [67]</td>
<td>During hormone therapy</td>
<td>Prostate</td>
<td>Supervised resistance exercise</td>
<td>60–70% of 1-RM, increase of 0.5 lb when &gt;12 repetitions were completed</td>
<td>3/week 2 sets 8–12 repetitions 9 exercises 12 weeks</td>
<td>155</td>
<td>Improvement in functioning in EG (2%) compared to WCG that showed a decline (3%)</td>
</tr>
<tr>
<td>Thorsen [58]</td>
<td>After chemotherapy</td>
<td>Mixed cancer diagnosis</td>
<td>Home-based aerobic programme, Walking and cycling.</td>
<td>Borg 13–15 60–70% MHR</td>
<td>Minimal 2/week, more were allowed At least 30 min 14 weeks</td>
<td>139</td>
<td>No differences in physical function (HRQoL) between EG (15%) and CG (14%)</td>
</tr>
<tr>
<td>Windsor [68]</td>
<td>During radiotherapy</td>
<td>Prostate</td>
<td>Home-based aerobic exercise / Walking</td>
<td>60–70% MHR</td>
<td>3/week 30 min 4 weeks</td>
<td>66</td>
<td>13.2% increase in walking distance (shuttle run test) in EG and a decrease (2.4%) in CG</td>
</tr>
</tbody>
</table>

Abbreviations: HRR: heart rate reserve; MHR: maximal heart rate; VO$_2_{max}$: maximal oxygen uptake; QoL: quality of life; EG: exercise group; (W)CG: (waiting list) control group; RG: relaxation group; PA: physical activity; PBSCT: peripheral blood stem cell transplantation; CML: chronic myeloid leukaemia; AML: acute myeloid leukaemia; NHL: non-Hodgkin’s lymphoma; MDS: myelodysplastic syndrome; UE: upper extremity; LE: lower extremity; RM: repetition maximum; SLBE: Symptom Limited Bicycle Ergometry; HW: high walkers; LW: low walkers; RT: radiotherapy; CT: chemotherapy; WD+: walking distance; N.S.: non significant; NA: no pre- or post-intervention data available. If exact pre and post-intervention data were available changes were expressed in % of baseline scores.
3.1.1. Aerobic exercise capacity

The evidence for improvement in aerobic exercise capacity or oxygen uptake was found on the level of meta-analyses [46], with moderate weighted mean effect sizes (WMES) of 0.51 during and 0.65 after cancer treatment [12]. Further analyses of studies included in Table 1 revealed fairly consistent effects meaning that all but one showed positive effects on aerobic capacity. The methodological quality of the studies varied from low to moderate. Due to variation in study populations, design and timing (during/after cancer treatment) and the relatively small number of studies, it was not possible to determine differences in effectiveness between the various programmes. With respect to the content it appeared that the programmes offered were quite similar. All programmes consisted of aerobic exercise modes such as cycling and walking [7,48–52,54,55,57,58], and two programmes combined cardiovascular training with muscle resistance training [53,56]. Most programmes used a moderate to high aerobic training intensity with a training heart rate at 50–80% of the maximal heart rate (MHR), at 50–80% of VO2max or at 50–70% of the heart rate reserve (HRR), in line with the ASCM guidelines [14]. In most cases, a training volume of 10–30 min was used and frequency varies between three times weekly to daily.

3.1.2. Muscle strength

No meta-analyses or systematic reviews were found on the effectiveness of exercise on muscle strength in cancer patients. For cancer patients, nine controlled studies (Table 2) were found that reported beneficial effects of aerobic exercise [73,75], PRE [67,70,74] or PRE in combination with aerobic exercise [53,56,69,72] on muscle strength. However, six of the nine studies were actually pilot studies with small numbers of patients. Because pre-intervention and post-intervention data were not available in five out of nine studies, it is not possible to determine differences in the effectiveness of the programmes. With respect to the content of the programmes it appeared that aerobic exercise consisted of walking or cycling with moderate to high intensity. PRE mostly consisted of the exercise of large muscle groups of the upper and lower extremities. Although the intensity of PRE should be based on the overload principle [14], weight settings were not precisely specified in most studies and varied from a fixed range of weights to the ability to lift weights until failure occurred in 8–20 repetitions. Only one study specified the intensity as moderate to high, based on 60–70% of 1-Repetition Maximum1 (1-RM) [67]. PRE was commonly performed in two to three sets with 8–12 repetitions per set. The majority of the sessions lasted 20–40 min with a frequency of two to four times weekly.

1 The 1-Repetition Maximum (1-RM) refers to the maximum load that a person is able to lift once. This maximum load is used to define the training intensity of progressive resistance exercise. The training load is based on a percentage of the 1-RM, depending on the training status of the patient.

3.1.3. Fatigue

The evidence for reduction in fatigue was found on the level of meta-analyses [46] with a small weighted effect size of 0.11 [44], but a zero effect size was also reported [45]. This inconsistency and the rather small effect size might be attributed to the variety of programmes aimed at the reduction of fatigue. Many studies had a small sample size and provided insufficient reports on the methodological criteria. Regarding the content (Table 3), aerobic programmes were described with intensity varying from moderate to high (at 50–80% MHR, at 50–80% VO2max or at 50–70% HRR) [48,50,59–62,65–68], to programmes that were self-paced [63,64] as well as programmes that were based on a ‘rate perceived exertion’ of 13–15 [52,58] on the Borg Scale [76]. The latter two might be less intensive and aimed less at improvement of aerobic capacity than the first programmes. However, based on the studies included, no differences in effectiveness could be determined, although a frequency of at least three times a week seemed to be associated with a positive effect on fatigue. In addition, one study reported positive effects of progressive resistance exercise on fatigue [67]. One study comparing aerobic training combined with PRE to placebo reported no significant differences in fatigue between the groups [62]. One study comparing aerobic exercise and relaxation reported equal beneficial effects on fatigue without differences between the groups [52]. The last aerobic training study reported no beneficial effect on fatigue, despite an improvement in VO2max, and attributed this to an overly high training intensity (60–70% MHR) [58]. Thus, with regard to fatigue, the results concerning the outcomes and the contents of the programmes are not consistent. Aerobic exercise may be beneficial but a high intensity does not seem necessary or may even have negative effects. The results may support the need for further research. Perhaps the multidimensional nature of fatigue requires other approaches, which is supported by a systematic review of the management of chronic fatigue syndrome that concluded that graded exercise therapy and cognitive behavioural therapy showed the most promising results [77].

3.1.4. Quality of life/physical role functioning

The evidence for the improvement of QoL in cancer patients was found on the level of meta-analyses [46] with a weighted effect size of 0.30 [12,44]. These effect sizes may be due to inconsistent findings across the various studies and/or variety in the content of the programmes. Table 4 shows that both aerobic exercise programmes with a moderate training intensity [49,50,54,57,65,66,68] and self-paced programmes [63,64] were effective in increasing physical role functioning. Another study, using low and moderate aerobic exercise, found beneficial effects on physical wellbeing, despite a lack of effect on aerobic capacity [48]. One study found that stretching exercises with no resistance training may be feasible for improving physical wellbeing [61]. Interestingly, one aerobic training study reported that despite physiological improvement, no beneficial effect on QoL, including physical functioning, occurred within the exercise group [58], and this was attributed to an overly high training intensity. Furthermore, programmes
RCTs reported on the beneficial effects of which can be tailored to either the individual or a group. Two based, which is most likely to be individual, or as supervised, exercise[14]. Most studies specify their intervention as home-which cycling may be the safest as it is a non-weight-bearing logs. Both cycling and walking programmes were used, of which cycling may be the safest as it is a non-weight-bearing exercise[14]. Most studies specify their intervention as home-based, which is most likely to be individual, or as supervised, which can be tailored to either the individual or a group. Two RCTs reported on the beneficial effects of a group exercise programme[52,59], and one of these considered that the effects of the programme may be attributed to the presence of support provided by peers[59]. The length of training programmes varied between three weeks and six months. Most studies presented used breast cancer patients, but positive findings were also found in patients with other types of cancer, such as leukaemia, stomach, prostate, colorectal and ovarian[15]. This may indicate that exercise is effective in a variety of cancer types. Furthermore, exercise is shown to be effective during and after completion of cancer treatment – both preventing deterioration and improving physical functioning.

3.1.4.1. Summary and conclusion concerning content. The level of evidence on the effectiveness of exercise on the reduction of physical problems varies according to the defined problem. Limited data are available on the effectiveness of exercise in cancer patients due to methodological shortcomings. Evidence supports the effectiveness of aerobic exercise on exercise performance (meta-analyses, moderate effect size). There is meta-analysis evidence on the effectiveness of exercise on fatigue and role functioning, but effect sizes are contradictory and small, respectively. Evidence on the effectiveness of progressive resistance exercise in cancer patients is promising (on the RCT level).

Concerning the content, two modalities of exercise are commonly described: aerobic exercise training and PRE. Aerobic training seems to have beneficial effects on aerobic capacity, fatigue and physical role functioning. PRE alone or combined with aerobic training may have a beneficial effect on muscle strength, fatigue and physical role functioning. Regarding the intensity, training programmes with a moderate to high intensity seem to be effective in improving aerobic capacity and muscle strength. Concerning reduction of fatigue and the improvement of physical role functioning, findings are not consistent and some argue against a high training intensity. Furthermore, aerobic training (cycling or walking) alone or combined with PRE seems to be effective and applicable to all defined problems.

3.2. Evidence concerning the delivery

3.2.1. Self-management/self-efficacy interventions and effectiveness

A search on the effectiveness of self-management and self-efficacy in cancer patients revealed one meta-analysis. This meta-analysis of social cognitive theory, including components addressing self-efficacy, expectations and self-regulation, showed that psychosocial interventions including these components had greater effects on QoL in cancer patients than interventions that involved fewer or no social cognitive theory components[78]. Additional searches on the effectiveness of self-management approaches as compared to controls and/or to routine care in other chronic diseases revealed eleven relevant meta-analyses which support the notion that self-management programmes are beneficial in controlling and preventing chronic disease complications. Self-management programmes appeared to have beneficial effects on health outcomes in diabetes[79–83,84], hypertension[79,85], cardiac [86], asthma/COPD [82,87,88] and arthritis [89] patients. However, no effect of self-management was reported in meta-analyses of osteoarthritis[79] and arthritis[82]. Most evidence suggests that self-management programmes and self-efficacy enhancing techniques are more effective compared to no intervention, and some evidence suggests that self-management is more effective compared to traditional care programmes.

3.2.2. Self-management/self-efficacy interventions and adherence to exercise, and adoption of physically active lifestyle

Adherence to and efficacy of exercise in cancer patients showed a linear dose response relationship; the higher the adherence the greater the efficacy of exercise[90]. It has been reported by the ASCM that two weekly sessions are needed to maintain and three to improve aerobic fitness[14]. However, adherence and compliance to physical training in cancer patients range from 52 to 89%[21]. In addition to exercise prescription, self-management programmes or self-efficacy enhancing techniques may also be relevant for adherence to and adoption of exercise. Self-management theory considers internal motivation as more effective for lifestyle change than external motivation (that is, ‘changing to please the physician’) [16]. The importance of self-efficacy for initiating and maintaining regular physical activity derives from social cognitive theory[19] and underlines the fact that efficacy beliefs are critical to the success in short-term structured exercise programmes due to their effect of enhancing adherence [91].

No meta-analyses were found on self-management/self-efficacy interventions related to exercise adherence and the adoption of a physically active lifestyle in cancer patients. One meta-analysis of cardiac patients revealed that self-management strategies were promising in improving cardiac rehabi-
litation uptake, adherence and/or lifestyle changes [86]. It was noted that performance self-efficacy seems to be more important in the early adoption phase of a clinical exercise programme, whereas self-regulatory skills are more important in the maintenance phase of exercise. This is in line with two meta-analyses of healthy elderly people, revealing that physical activity may lead to mastery experiences that can increase the level of self-efficacy [92], which may in turn have a moderating and positive effect on physical activity [93]. A third meta-analysis using the trans-theoretical model (TTM) of behaviour change revealed that changes in self-efficacy were moderately consistent with the predictions of TTM in the physical activity domain. Thus, self-efficacy was associated with exercise behaviour [94]. In colorectal cancer patients, a RCT reported that programmed exercise and perceived success – which can elevate levels of self-efficacy – were predictors of post-programme exercise [95]. Two RCTs also found that self-efficacy was a mediator of later physical activity in cardiac patients [96] and healthy elderly people, and the latter study additionally reported that two dimensions of self-efficacy were important for exercise adherence: the level of self-efficacy at baseline and the amount of change in self-efficacy [97].

Because behavioural changes, such as developing a physically active lifestyle, may require that adequate perceptions concerning the illness already exist, we performed an additional search on illness perceptions. The notion of illness perceptions is derived from the self-regulation theory that proposes that individuals construct schematic representations of illness [98]. Such representations or perceptions include five related but conceptually and empirically distinct components: identity (label and symptoms), timeline, cause consequences and curability/controllability. One meta-analysis of diverse patient populations revealed that a stronger perception of identity, timeline and consequences was associated with passive coping and lower functioning [99]. In contrast, patients who perceived high controllability seemed to have more active coping styles and better functioning than those with perceived low controllability [99]. Furthermore, several RCTs reported the beneficial effects of therapeutically manipulated illness perceptions on coping and QoL in patients with myocardial infarction and cardiac surgery patients [100].

3.2.2.1. Conclusion concerning the delivery. Regarding the delivery, there was some evidence that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the QoL in cancer patients, and on exercise adherence and later exercise behaviour.

3.3. Presentation of the programme

In the present section we will first describe how the programme was designed. Then, we will describe the actual programme in general terms. Appendix A describes the programme in more detail, including information on the treatment elements during the various phases of the programme.

According to the principles of intervention mapping, we first formulated four individual proximal programme objectives: ‘improvement of aerobic exercise’, ‘improvement of muscle strength’, ‘reduction of fatigue’, and ‘improvement of physical role functioning’. Because we considered a low activity pattern a maintaining factor for all problems, we additionally formulated one proximal programme objective for the group as a whole: ‘adoption of a physically active lifestyle’. Programme objectives were formulated as programme modules. Next, we selected theory-based interventions based on the review, including aerobic exercise training and progressive resistance training, self-management and self-efficacy enhancing techniques. Practical strategies for the content were based on the results of the present review. With regard to the improvement in aerobic capacity and muscle strength, the evidence found was at the meta-analysis level with a moderate effect size and at the RCT level. We therefore used the information obtained from the programmes included in the review for the content of these modules. This information was in line with the recommendations of the American College of Sports Medicine [14] for exercise in healthy adults and principles of exercise training. The ACSM describes a training intensity ranging from moderate to high. With regard to the reduction in fatigue and improvement of physical role functioning, the evidence at the meta-analysis level had zero and/or small effect sizes and was thus ambiguous. We therefore followed the recommendations of the ASCM for the content of these modules and adapted these in line with the finding from the review that a high training intensity may have a negative effect on outcome. Accordingly, for the reduction in fatigue and improvement of physical role functioning we included a lower training intensity at the start and a more gradual increment of intensity during the programme than is required for training aerobic capacity and/or muscle strength. Practical strategies for the delivery, including enhancing self-management and enhancing self-efficacy – for which the evidence found was at the meta-analysis level – were based on literature [101,102] and on suggestions from experts (see actual programme). In the final programme, the main principles of exercise training, self-management, and self-efficacy enhancing techniques were combined, and this train of thought is visualized in Fig. 1.

An additional consideration regarding the delivery of the programme, which was not taken into account in the review, was the choice between an individual and a group approach. The efficacy of exercise may be higher if the training is personalized. However, the question could be posed whether personalized training should automatically imply individual training or whether a group approach is also applicable. A group approach might be preferred because peer contact provides opportunities for social support [103], social comparison [104] and modelling [105], which can also have positive effects on self-efficacy [19]. The latter may in turn mediate physical [106] and mental health [107], and importantly, behaviour associated with physical activity [97]. In addition, social support processes seem to engender changes in lifestyle [108]. Finally, group programmes might be interesting because of cost-effectiveness. A meta-analysis that
examined the effect of psychological interventions on anxiety and depression in breast cancer patients concluded that group therapy is at least as effective as individual therapy [109]. A meta-analysis of self-management in diabetes showed that lifestyle interventions were generally more effective in group settings, whereas skills teaching was effective in individual and group settings [110].

A final point concerning the delivery may be the ‘transfer’ of local exercise training into daily activities. For example, muscle strength training may have significant positive effects on muscle strength and endurance and on physical functioning, but it is known that without the integration of functional training, improved muscle strength does not consistently result in improved functional task performance [111]. To undertake most daily activities an individual must be able to perform basic movements and also combinations of these in order to accomplish more complex tasks [112]. Sports may provide training in such complex tasks. Sports are often included in rehabilitation programmes to facilitate their integration into daily life, as it is more difficult to become physically active when sedentary [113]. Enjoyment of sport has also been reported to be a mediator for the adoption of an active lifestyle [93]. A Cochrane review reported that playing sport might have a favourable effect on physical activity levels and physical health, help develop sport-specific skills, provide a sense of achievement and empowerment, develop self-esteem and teach self-discipline [114].

3.3.1. The actual programme

Regarding the content of the programme we developed a supervised exercise programme, consisting of four separate modules tailored to the individual patient’s most prominent problem. These modules are formulated in terms of individual goals: (1) improvement of aerobic capacity, (2) improvement of muscle strength, (3) reduction of fatigue, and (4) improvement of role functioning. The four modules contain two personalized treatment modalities including aerobic exercise training and PRE, which differ in intensity depending on the problem. The intensity of the programme is moderate to high in modules 1 and 2 and low to moderate in modules 3 and 4. The intensity of aerobic exercise and the PRE is prescribed on the basis of the MHR and the 1-RM in line with the ASCM guidelines [14]. With respect to aerobic exercise training, we chose a cycling programme because it is non-weight-bearing and, therefore, the safest exercise mode. PRE includes various exercises for the large muscle groups of the lower and upper extremities using machine resistance and/or free weights. Training sessions are 20–30 min duration for the aerobic cycling programme and 10–
20 min duration for the PRE. The entire programme takes 12 weeks. An overall goal was formulated as ‘adopting a physically active lifestyle’, which was provided as a group module.

Based on the results regarding the delivery we adjusted the programme along the following lines. Acknowledging the value of personalized exercise programmes, and recognizing the potential advantages of group therapy we developed the physical training programme as a group programme in which the individual is able to work towards his or her own goals. Thus, the group as a whole performs aerobic exercise and progressive muscle strength training, but the individual exercise modules are tailored to individual problems and are therefore prescribed individually. Based on the potential advantages of sport we included group sports in addition to individual aerobic exercise training and progressive resistance exercises.

Regarding the results on adherence and exercise prescription, we chose to deliver the cycling exercise programme and the PRE twice a week under supervision, and extended this with an aerobic home-based walking programme that allows for an increase in the frequency from once a week to daily. In addition, due to the evidence suggesting that self-management programmes and self-efficacy enhancing programmes have beneficial effects on functioning in chronic diseases, on QoL in cancer patients, and on exercise adherence and later exercise behaviour, we integrated self-management and self-efficacy enhancing techniques into the programme. Because self-efficacy is enhanced through mastery experiences, vicarious experiences, verbal persuasion and physiological feedback [19], these sources are systematically manipulated during the aerobic exercise training, the PRE and the sports undertaken. First, a low intensity at the start of the programme is included to assure that all participants are able to complete the training, and thus will experience a feeling of mastery that may increase self-efficacy. Secondly, verbal persuasion is provided by the therapist by strongly encouraging the patient to perform the training activities. Thirdly, the programme is deliberately delivered as a group programme to enhance vicarious learning and the potential modelling effects thereof. Finally, the physiological arousal is supposed to be felt by the patient through the improvement in their exercise capacity. Self-management is integrated into the programme by including the six phases in the self-management process [18] in the physical exercise programme and sport. These were goal setting, which seems to fulfil a crucial role in rehabilitation [115] and is an important determinant of actual performance, motivation for change, and improving self-efficacy in specific situations [78,116] followed by information collection through self-monitoring (for example, checking heart rate, scoring Borg Scale and Visual Analogue Scale’, using an exercise log); information processing and evaluation, involving detection of change, and evaluation of information against norms such as heart rate or Borg Scale; decision-making, deciding on performance of activities, action, the actual performance of self-management activities such as exercise; and self-reaction, the evaluation of performance by providing feedback [18]. In addition, we included attention to illness perceptions during the programme because rational perceptions were considered to be a prerequisite for active coping and behavioural change.

4. Discussion and conclusion

4.1. Discussion

The present paper describes the development of a physical training programme for cancer patients. Four related but conceptually and empirically distinct physical problems were described, including decreased aerobic capacity, decreased muscle strength, fatigue and impaired role functioning, all probably the result of low physical activity. The paper aimed to identify the optimal content for an exercise programme that addresses the four physical problems, based on the highest level of evidence available. The results of the review showed that many studies had insufficient reports on the methodological criteria, which complicated drawing conclusions. The quality of several studies was due to small sample sizes or lack of a randomization procedure. Evidence supports the positive effects of exercise on physiological outcome such as exercise capacity during and after completion of cancer treatment. The results for the effectiveness of exercise on fatigue and/or physical role functioning are ambiguous. The results of the effectiveness of PRE on muscle strength are limited but promising. Thus, the level of evidence on the effectiveness of exercise on the reduction of physical problems varies according to the defined problem, and evidence increases when moving from muscle strength (RCT level), fatigue (meta-analysis with low or zero effect sizes) and physical role functioning (meta-analysis with small effect sizes) to aerobic capacity (meta-analyses, moderate effect size). The paper further aimed to review the evidence available on the delivery of the programme. The study revealed some evidence (meta-analyses) that self-management programmes and self-efficacy enhancing programmes have beneficial effects on health outcomes in a variety of chronic diseases, on the QoL in cancer patients, and on exercise adherence and later exercise behaviour.

The final programme was developed applying the principles of intervention mapping. Although this is a frequently used method for developing theory and evidence-based health education programmes, the second step in the method was difficult. Indeed, our original intention was to include the ‘highest level’ of evidence only, but the evidence found appeared to be limited and ambiguous. For two modules, i.e., improvement in aerobic capacity and muscle strength, we included information from the review that was also in line with the ACSM guidelines. Because the evidence for the remaining modules (fatigue and role functioning) was ambiguous, we adapted the ACSM guidelines with ‘suggestions’ obtained from the review. The final programme was therefore based on the best available evidence.

The programme presented has been developed for cancer patients with the most frequently reported problems and is tailor-made. The intention is that patients be screened on their eligibility, prior to the programme. However, the programme is
not aimed at reducing specific tumour-related problems such as impaired shoulder function, lymphoedema, or problems due to amputation, and this was not the scope of the article either. Nonetheless, we are of the opinion that within the present programme more attention can be paid to patients with specific tumour-related problems. In particular, the self-management approach provides many opportunities for this. For example, patients can be invited to set goals in terms of improved functioning considering their own tumour-related problems. In addition, it seems possible and appropriate to combine the proposed exercise self-management programme with other interventions, such as diet or psychotherapy, as these interventions may also have positive effects on physical fitness.

4.2. Conclusion

Limited data are available on the effectiveness of exercise in cancer patients. Evidence supports the positive effects of exercise on aerobic capacity during and after completion of cancer treatment, while the effects on fatigue and physical role functioning are ambiguous and smaller. Programme descriptions for aerobic capacity are rather uniform, whereas programme descriptions for fatigue and physical role functioning usually differ. Some evidence supports the positive effects of self-management programmes and self-efficacy enhancing programmes on health outcomes, exercise adherence and later exercise behaviour.

4.3. Practice implications

The resulting programme was developed on the basis of the highest quality of evidence available regarding content and delivery. The content of the programme is based on information obtained from the review and on recommendations of the American College of Sports Medicine. Potential advantages of the programme are: (a) tailored physical training towards focusing on the patient’s established problems; (b) delivery of the training as a self-management programme that might have beneficial effects on outcome, adherence and a long-term physically active lifestyle. A randomized controlled trial (the Oncorev study) is currently ongoing and designed to examine the effectiveness of the physical training programme on exercise capacity, muscle force, fatigue and physical role functioning.

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Appendix A. A detailed description of the programme: phases and treatment ingredients

The self-management and tailor-made physical training programme is preceded by a physical assessment, which defines a patient’s problems and needs by assessing exercise capacity (Symptom Limited Bicycle Ergometry, SLBE) [117], testing muscle strength (1-RM test) [118] and anamnestic. The SLBE is considered to be the most precise measure of cardio-respiratory fitness and is recommended for use in order to determine a patient’s objective or subjective reduction in exercise capacity and prescribe the intensity of the aerobic bicycle training programme [14]. A 1-RM test is performed to determine maximal muscle strength as an indicator of the intensity of the progressive resistance exercise [14]. Additional information about the patient’s reduction in exercise capacity, functioning and activity pattern is obtained by an extended anamnesis, to establish whether and to what extent a patient suffers from the following: decreased aerobic capacity, reduced muscle strength, fatigue or limited physical role functioning. The anamnestic further includes exploration of the presence of irrational illness perceptions [99], and the patient’s expectations and goals [115] according to the self-management approach.

Before the exercise programme starts, an education session is held to acquaint the patient with peers, therapists and the therapeutic surroundings. Patients are informed about the programme’s rationale of physical training, self-management processes and illness perceptions. Patients are told that physical training has the potential to break through the vicious circle of physical cancer-related problems [15], and that self-management considers the patient’s responsibility to be central, whereas the role of the therapist is that of a guide. Patients have to commit themselves to this approach [18] and are invited to define their self-management goals as a necessary condition for behavioural change [17]. Finally, it is explained to the patient that rational illness perceptions [100] are the prerequisite for adequate and active self-management behaviour, and they are asked to explore their perceptions [99].

In the tailoring phase, the intervention is divided into an Individual Physical Training (IPT) programme and a group-oriented Sports and Games (SGP) programme, both supervised by a physical therapist. The IPT includes four individual modules tailored to individual problems and consists of improvement of (1) oxygen uptake/aerobic capacity, (2) muscle strength, (3) fatigue, and (4) physical role functioning. The four modules all use aerobic bicycle exercise training and progressive resistance training, which differ in intensity. The aerobic training is based on the maximal heart rate reached during the SLEB test. The training heart rate (THR) is computed by using the Karvonen formulae [119]. Progressive resistance muscle training of the trunk and the lower and upper extremities are performed and is based on the individual 1-RM [120].

The first four weeks of the IPT are used to verify the patient’s main problem defined at intake and their physiological response to training [14] in order to establish the most optimal training...
module. The aerobic training is performed at a THR of HR_{rest} + 30–50% (HR_{max}–HR_{rest}) over 20 min. Progressive resistance muscle training starts at 30% of the 1-RM, with a frequency of 10–20 repetitions over three series. Illness perceptions are individually explored and their effect on active behaviour is generally discussed in the group. Two processes of self-management are practiced, including goal setting [78,121] and monitoring [18]. Goals should be self-generated and positively formulated, otherwise motivation will fade [17]. Therefore, patients are invited to set specific, measurable, adequate, realistic and time-related (SMART) goals. Monitoring includes measuring the heart rate, scoring the Borg Scale for fatigue and dyspnoea before and following exercise, and using an exercise log. Successful performance accomplishment as a source of self-efficacy [19,101] is achieved by a low training intensity in the first four weeks, providing the opportunity for all patients to perceive success.

During weeks five to twelve aerobic bicycle exercise training continues at a THR of HR_{rest} + 50–80% (HR_{max}–HR_{rest}). The progressive resistance training increases from 30% of the 1-RM by 5–10% up to 50–65% of 1-RM. Intensity and progression of both training modalities differ between modules and are moderate to high in modules 1 and 2, and mild to moderate in modules 3 and 4. Training sessions are 30–45 min long with 20–30 min of aerobic training and 10–15 min of muscle resistance training. Patients are advised to have at least one additional aerobic training session a week, using a home-based walking programme. The walking programme [122] starts in week six with 5–10 min walking, which increases to 20 min by the end of rehabilitation. Furthermore, all six processes of self-management are included in each module. Thus, in addition to goal setting [121,123] and monitoring, patients evaluate their scores against the norm provided [18], and undertake action in the form of physical training applied to their problem [15]. Finally, self-reflection [18] is accrued by visual and oral feedback, such as graphics combined with reflective questions by the physical therapist.

Irrational illness perceptions which are revealed in weeks one to four are challenged by providing information, raising doubt, and providing alternative perceptions [124]. Information about the application of physiological training principles in cases of cancer-related problems is provided to all patients so as to change irrational perceptions about exercise and cancer. Patients with fatigue as their main problem (module 3) further receive an illustrative ‘model of fatigue’ that explains fatigue as a multidimensional construct with different physical and psychological determinants [4]. These patients are encouraged to undertake physical activity to increase their exercise capacity gradually without ‘centralizing’ fatigue, which may be considered as a cognitive behavioural technique of the therapist. Patients who have problems with role functioning (module 4) are taught how to restore the balance between ‘demand’ and ‘capacity’ during tasks and activities [125]. Exercise is combined with information about the ‘demand and capacity model’ in order to reach a better understanding of methods to reduce ‘demand’ by reducing activities that cause fatigue, and to increase the ‘capacity’ by graded exercise [15,126]. Finally, self-efficacy enhancing techniques are applied, such as a patient’s perceived mastery experiences, a therapist’s verbal persuasion, and vicarious experiences of peers regarding the ability to perform exercise tasks and recognize an improved physiological status such as a decrease in heart rate during exercise [19,101].

The GSP includes 24 one-hour sessions over twelve weeks with various sports and games such as indoor hockey, curling and badminton that stimulate patients to engage in and to enjoy sports, both aimed at improvement through a physically active lifestyle. In line with the IPT, the GSP is based on a self-management approach. Patients are invited to set SMART goals alongside the overall goal of increasing their activity level during leisure time [121,123]. Patients complete a Visual Analogue Scale to monitor their level of enjoyment during sport or games [18]. Action is fulfilled through the actual engagement in sport and games. Self-reflection is stimulated through reflective questions by the therapist. The GSP also includes, if necessary, attention to irrational perceptions [124] that may be barriers to the adoption of an active lifestyle. Furthermore, the GSP module has a fixed structure, including warming-up, main part and cooling down, aimed at an increase in self-efficacy [19]. During warming-up, basic elements of the sports that will be performed during the main part are practised. The main part contains the actual sport performance and uses already learned movements in the sport and game activities, allowing patients to perceive success more easily. Peers are invited to engage in sport together so that modelling experiences may occur. Therapists guide these processes and use verbal techniques to persuade patients to engage in sport or games. Afterwards a cooling-down period takes place using relaxation techniques to lower physiological arousal [19].

References


Hayes S, Davies PS, Parker T, Bashford J. Total energy expenditure and body composition changes following peripheral blood stem cell transplantation and participation in an exercise programme. Bone Marrow Transplant 2003;31:331–8.


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