

**A systematic review and narrative synthesis to explore the effectiveness of exercise based interventions in improving fatigue, dyspnoea and depression in lung cancer survivors**

**C. Henshall**

**L. Allin**

**H. Aveyard**

**Department of Nursing, Oxford Brookes University**

## 1 **Background**

2 Cancer is, for many, a long term condition, as advances in new cancer treatments mean that  
3 survival rates are increasing <sup>1</sup>, with half of people diagnosed in England and Wales surviving  
4 for ten years or more <sup>2</sup>. However, cancer survivors' psychological and physical wellbeing can  
5 be negatively affected post cancer due to the multitude of symptoms and side-effects they  
6 incur from cancer and its treatment <sup>3</sup>.

7 There are around 47,000 new cases of lung cancer in the UK each year <sup>2</sup>; many of these  
8 people have significant smoking related co-morbidities <sup>2</sup> which can negatively impact on  
9 their activities of daily living and subsequent quality of life. Lung cancer patients may  
10 undergo curative treatment procedures, including surgery, chemotherapy and radiotherapy;  
11 these treatments, whilst potentially life-giving, are associated with a number of frequently  
12 reported and connected symptoms, such as fatigue, dyspnoea and depression, which can be  
13 long lasting and debilitating <sup>4-6</sup>.

14 Fatigue is the most prevalent and disruptive symptom post treatment in cancer patients,  
15 affecting between 57-100%, whilst depression is present in around one third <sup>6</sup>. In addition,  
16 dyspnoea can substantially add to the onset of fatigue <sup>6</sup>. The presence of these symptoms,  
17 which can be made worse by surgery and/or adjuvant radiotherapy and chemotherapy, can  
18 have negative implications on the psychological and physical wellbeing of lung cancer  
19 survivors <sup>6</sup>. The presence of fatigue, dyspnoea and/or depression can inhibit lung cancer  
20 survivors activities of daily living, increase their social isolation, decrease their health and  
21 fitness levels and impair their return to work ability <sup>6-9</sup>, making them more likely to access  
22 healthcare services for support and management of their condition.

23 Lung cancer patients have been reported to experience more symptom distress than patients  
24 with other types of cancer, with profound effects on their emotional and physical wellbeing

25 <sup>10, 11</sup>. Fatigue, depression and dyspnoea are among the most common symptoms for lung  
26 cancer patients, and are often interrelated, with many patients experiencing a combination of  
27 symptoms <sup>12, 13</sup>. This can interfere with patients' activities of daily living, with more  
28 interference occurring as symptom severity increases <sup>10</sup>.

29 Growing appreciation of the extent to which the mind and body are linked <sup>10, 11</sup> indicates that  
30 depressive symptoms may exacerbate symptoms of fatigue and dyspnoea, and vice-versa.  
31 This supports the hypothesis that depression may be either the sequela *or* the precursor to  
32 uncontrolled physical symptoms such as fatigue and dyspnoea <sup>10, 11</sup>. Poor psychological  
33 health is associated with lower physical functioning, suggesting that psychological and  
34 physical health outcomes are inter-related <sup>12, 13</sup>. Hence, strategies aimed at improving any one  
35 of the symptoms of depression, fatigue or dyspnoea, may incur benefits across all three <sup>10</sup>.

36 Lung cancer survivors use a variety of coping strategies to help to control their symptoms <sup>14</sup>.  
37 Exercise is one such strategy, helping lung cancer survivors to regain or maintain physical  
38 fitness following their cancer diagnosis <sup>11</sup>. This is illustrated by evidence that lung cancer  
39 patients with higher performance statuses have better physical and psychological outcomes  
40 than those with lower performance statuses <sup>11</sup>. Recent guidelines recommend that individuals  
41 with cancer should be as physically active as possible, 'avoid inactivity' <sup>15, 16</sup> and that any  
42 prescribed exercise should be individualised in accordance with cancer survivors' pre-  
43 treatment fitness levels and symptom burdens <sup>15</sup>.

44 Research has suggested that exercise is the most common form of self-management practice  
45 used post-cancer treatment <sup>17</sup>, with people using it for a variety of reasons, including to regain  
46 health and fitness, improve treatment side-effects, relax the mind and body and to regain a  
47 sense of normality post-cancer <sup>9</sup>. Many self-management programmes including an exercise  
48 component have shown improvements in cancer patients' levels of self-efficacy,

49 empowerment, quality of life, coping mechanisms, healthy behaviours and symptoms such as  
50 fatigue, dyspnoea and depression<sup>18-25</sup>. In addition exercise has been found to be a protective  
51 factor for fatigue<sup>6, 26, 27</sup>. These findings are strengthened by two recent meta-analyses which  
52 recommend physical exercise in the management of several cancers, including lung cancer<sup>22</sup>,  
53<sup>23</sup>. In addition the National Institute for Health and Care Excellence (NICE) recommend that  
54 people with mild to moderate depression and chronic physical health problems undertake  
55 physical activity programmes<sup>28</sup>, emphasising the role of exercise in improving health  
56 outcomes for those living with long term conditions. Similarly, the American Cancer Society  
57<sup>25</sup> and the National Comprehensive Cancer Network<sup>24</sup> both recommend routine physical  
58 activity in lung cancer patients.

59 Though much research has focused on the effects of exercise in improving the health  
60 outcomes and quality of life in cancer patients<sup>21, 29</sup>, the majority has focused on breast cancer  
61 survivors and have been conducted during treatment<sup>30</sup>. Despite similarities existing between  
62 lung cancer patients and those diagnosed with other types of cancer, there is a need to  
63 examine literature focusing specifically on lung cancer survivors. Lung cancer survivors may  
64 experience greater symptom distress than other types of cancer survivor<sup>10, 11</sup> and have  
65 distinct characteristics, with lung cancer rates consistently higher among men, older people,  
66 smokers and those with lower socio-economic statuses<sup>31</sup>. Hence research into the most  
67 suitable exercise interventions for lung cancer survivors is required, to ensure that their  
68 symptoms are better controlled and that tailored exercise interventions are designed to meet  
69 their specific needs.

70 One systematic review exploring non-invasive interventions in improving wellbeing and  
71 quality of life in patients with lung cancer found exercise to have beneficial effects on self-  
72 empowerment and physical strength, but no improvement in quality of life<sup>32</sup>. Another  
73 review examining the effect of exercise training on lung cancer patients within 12 months of

74 lung resection found that exercise training may increase the exercise capacity of this  
75 population group<sup>33</sup>. No studies, to our knowledge, have examined the effects of different  
76 types of exercise interventions on fatigue, dyspnoea and depression in lung cancer survivors,  
77 despite these symptoms being commonly experienced by them<sup>4, 5, 34</sup>, highlighting an  
78 important gap in the literature. This is an important area to examine as less than a third of  
79 lung cancer survivors meet recommended physical activity guidelines<sup>35</sup>, indicating that more  
80 must be done to uncover which exercise interventions may be useful to them. A  
81 comprehensive literature review can help determine whether certain exercise types are more  
82 effective than others in managing symptoms for lung cancer survivors<sup>36</sup>.

83 Thus, this systematic review will aim to examine the evidence on the effects of exercise  
84 based interventions on fatigue, dyspnoea and/or depression in lung cancer survivors. Though  
85 the term ‘cancer survivor’ can be associated with people living with cancer at different stages  
86 of the cancer pathway, for the purpose of this study ‘cancer survivor’ refers to lung cancer  
87 patients who have finished their active treatment for cancer. A quantitative narrative  
88 synthesis will be undertaken to help to describe, explain and interpret the study findings and  
89 to attempt to find explanations for these findings<sup>37</sup>.

90

## 91 **Methods**

92 The PRISMA guidelines and flow diagram were followed<sup>38</sup>. Ethical approvals were not  
93 required.

94

95

96

97 **Criteria for considering studies for this review**

98 **Types of studies/interventions**

99 All randomised or quasi-randomised controlled trials (RCTs), observational studies and  
100 qualitative studies were considered for inclusion if they focused on the effectiveness of  
101 exercise interventions in improving symptoms of fatigue, dyspnoea and/or depression in lung  
102 cancer survivors. Lung cancer survivors must have received the exercise intervention for the  
103 study to be eligible for inclusion.

104 **Types of participants**

105 Studies were excluded if the majority of participants in the study were cancer patients, rather  
106 than survivors. Participants were considered to be cancer patients if they were still  
107 undergoing active treatment (surgery, chemotherapy, radiotherapy) for cancer at the time of  
108 undertaking the study intervention. Studies reporting on exercise interventions in cancer  
109 survivors were excluded if none of the participants were lung cancer survivors, or if  
110 participants were less than 18 years of age.

111 **Search methods for identification of studies**

112 The databases CINAHL, MEDLINE, EMBASE and the Cochrane Database were searched  
113 between January-May 2017. Both text and indexed terms (MeSH) were used in line with the  
114 relevant database search engine systems. The search strategy used is outlined in figure 1.  
115 Google and Google Scholar were also searched for any relevant unpublished studies and  
116 reference lists of all full text articles included in the review were checked in case they  
117 identified any potentially relevant articles. Any relevant systematic reviews were also  
118 examined to see if any papers making up the reviews were eligible for inclusion.

119 Searches were limited to papers published in the English language from the year 2000  
120 onwards as developments in cancer treatments have evolved in the last two decades<sup>39</sup>. As  
121 such the symptoms experienced by lung cancer patients may be of a different nature and  
122 severity, affecting the impact of any subsequent exercise interventions and limiting the  
123 relevance of studies published before this time.

#### 124 **Selection of studies**

125 All of the studies were screened for inclusion in the review, based on the eligibility criteria  
126 outlined above. Studies were included in the review if some (or all) of the participants were  
127 lung cancer survivors.

#### 128 **Data extraction and risk of bias**

129 Data from the included studies was extracted independently, discussed and summarised by  
130 two researchers (CH, HA) using a study specific extraction form which was designed to  
131 collect all the relevant study data. The characteristics of the studies are summarised in Table  
132 1. The quality of the included studies was assessed by CH and discussed with HA, using the  
133 appropriate Critical Appraisal Skills Programme Checklists<sup>40</sup>. Any uncertainty about the  
134 level of bias attributed to an individual study was discussed until a consensus was reached. It  
135 was not necessary to contact authors of the included studies to obtain any more detailed study  
136 information.

#### 137 **Data synthesis**

138 All of the studies included in the review were quantitative and this data was descriptively  
139 summarised. However, due to the different study designs and the varying quality of the  
140 statistical data in many studies, it was not appropriate to undertake meta-analyses of the  
141 dataset, as a pooling of results across the studies was not possible.

142 **Results**

143 **Characteristics of studies**

144 852 records, titles and abstracts were initially screened for inclusion in the review, of which  
145 797 were excluded, leaving 54 remaining after the exclusion of any duplicates (n=14). Of  
146 these, 44 were excluded once the full articles were assessed for eligibility, leaving 10 for  
147 inclusion in the final review <sup>41-50</sup> (Figure 1).

148 Characteristics of the 10 studies included in the review are shown in Table 1. Seven studies  
149 included only lung cancer survivors <sup>43-46, 48-50</sup>, whilst three also included other cancer types <sup>41,</sup>  
150 <sup>42, 47</sup>. In total 516 cancer survivors were included in the review, of which 298 (58%) were  
151 lung cancer survivors. The number of participants in the studies ranged from 10 to 162. The  
152 cumulative drop-out rate across the studies was 74 (14%). Seven studies had prospective,  
153 single site, pre/post-test designs <sup>41, 43, 45, 46, 48-50</sup>, whereas three were RCTs <sup>42, 44, 47</sup>. Of these  
154 two were single site <sup>42, 44</sup> and one was multisite <sup>47</sup>, taking place at three hospital outpatient  
155 departments. The studies took place in a range of settings including hospital inpatient and  
156 outpatient departments, community based and home based settings. All study participants had  
157 previously received cancer treatment consisting of either surgery, radiotherapy,  
158 chemotherapy, or a combination of these. The age of participants ranged from 30 to 80 (age  
159 range was not reported in one study <sup>43</sup>). Five studies were carried out in Europe, three in  
160 North America, one in Canada and one in Australia. All studies were published between 2004  
161 and 2017.

162 **Risk of bias in included studies**

163 Overall, seven studies were deemed to have a high risk of bias <sup>41-43, 45, 48-50</sup>, two an unclear  
164 risk of bias <sup>44, 46</sup> and one a low risk of bias <sup>47</sup>. Common reasons for this high level of bias

165 were related to flaws in the study design, such as selection bias, small sample sizes, lack of  
166 blinding and randomization methods and a lack of rigour in data analysis techniques, such as  
167 not accounting for confounding factors and a lack of reporting of confidence intervals. The  
168 substantial proportion of studies with a high or unclear risk of bias was deemed sufficient to  
169 affect the interpretation of the results from the review.

## 170 **Description of studies**

### 171 **Pre/post-test study designs**

172 Seven studies used single site, pre/post-test designs. One of these studies measured  
173 depression as an outcome measure<sup>48</sup>, whilst four measured dyspnoea<sup>43, 48-50</sup> and six fatigue  
174<sup>41, 45, 46, 48-50</sup>. The first of these studies aimed to measure the extent exercise impacted on  
175 fatigue, physical and psychosocial wellbeing and the quality of life of female cancer  
176 survivors<sup>41</sup>. The exercise intervention consisted of an oncology community outreach  
177 program offering a 'Get fit, stay fit' programme, with twice weekly low impact aerobics,  
178 toning, flexibility exercises and relaxation techniques. The second study<sup>43</sup> explored the  
179 effects of an inpatient multi-disciplinary team pulmonary rehabilitation programme on  
180 dyspnoea, pulmonary function and exercise capacity. The rehabilitation programme included  
181 a five hour educational seminar by a qualified health professional which incorporated chest  
182 physiotherapy and breathing techniques for dyspnoea, 30 minute respiratory physiotherapy  
183 sessions five times per week, 25 minute supervised cycling sessions three to five times per  
184 week and 30 minutes of gymnastics daily that focused on general mobilization and flexibility.  
185 Participants were also instructed to walk for one hour per day.

186 The third study<sup>45</sup> also examined the outcome of a pulmonary rehabilitation programme and  
187 measured its effects on fatigue, quality of life and exercise capacity in lung cancer survivors.

188 The exercise programme was supervised by a physiotherapist and took place three times a

189 week for 12 weeks. It included two 90 minute resistance and endurance training sessions on  
190 cycle ergometers and treadmills. In week three, participants trained for 60 minutes, using  
191 activities of daily living, such as walking up stairs, regulating breathing during different  
192 postures and activities, playing tennis or cycling. The programme additionally included five  
193 sessions of relaxation exercises and breathing regulation techniques.

194 The fourth study <sup>46</sup> examined the effects of supervised aerobic exercise training on fatigue  
195 and aerobic fitness among lung cancer survivors who had undergone surgery. The  
196 programme was individually tailored to each participant and all sessions were supervised by  
197 sports medicine exercise specialists. Exercise consisted of three aerobic cycle ergometry  
198 sessions per week on non-consecutive days for 14 weeks.

199 The fifth study <sup>48</sup> aimed to evaluate the feasibility and efficacy of a progressive resistance  
200 exercise training programme in lung cancer survivors, which included leg and chest presses,  
201 seated rows, leg extensions, leg curls, shoulder presses, lateral pull downs and abdominal  
202 exercises, with 90-120 seconds rest between each exercise. The sessions were supervised by a  
203 qualified exercise physiologist and depression, fatigue and dyspnoea were measured.

204 The sixth study <sup>49</sup> aimed to assess changes in dyspnoea, fatigue, exercise capacity and quality  
205 of life of lung cancer survivors before and after a 28 day inpatient rehabilitation training  
206 programme which included cycle ergometer exercises in intervals of three to five minutes for  
207 30 minutes daily. This was complemented by oncological rehabilitation measures including  
208 health education techniques. In addition, clinical counselling and medical supervision, drug  
209 based therapies and psychological support were offered.

210 Finally, the last study <sup>50</sup> aimed to examine the effects of an inpatient multi-disciplinary  
211 rehabilitation programme on dyspnoea, fatigue, pulmonary function and exercise capacity in  
212 lung cancer survivors. The programme was supervised by a physiotherapist and took place

213 over eight weeks, for one to two hours per day. It consisted of ergonomic cycling, treadmill  
214 walking, weight training and gymnastics.

### 215 **Randomised controlled trials**

216 All three RCTs, measured fatigue as an outcome measure<sup>42, 44, 47</sup>, one measured dyspnoea<sup>42</sup>  
217 and one depression<sup>47</sup>. The first RCT aimed to compare the effect of aerobic exercise and  
218 progressive relaxation training on dyspnoea, fatigue, quality of life and the physical  
219 performance of cancer patients recovering from surgical treatment<sup>42</sup>. It consisted of 30  
220 minutes cycle ergometer training for five days per week, over three weeks. The relaxation  
221 training consisted of a systematic programme of contraction and relaxation of different  
222 muscle groups.

223 The second RCT<sup>44</sup> aimed to investigate the effects of an exercise and balance programme  
224 compared to normal medical care on cancer related fatigue severity and fatigability in lung  
225 cancer survivors. The intervention group involved a nurse supported (via phone calls and  
226 home visits) home exercise intervention using the Nintendo Wii Fit Plus and consisted of  
227 light intensity walking and balance exercises that corresponded to usual activities of daily  
228 living. Wii walking was self-paced and comfortable. Exercise duration started at five minutes  
229 per day and built by five minutes each week with the goal of walking 30 minutes per day by  
230 week six. Balance exercises were also undertaken each day from weeks one to six.  
231 Participants self-reported their activity levels. The control group received usual medical  
232 follow up care from their medical providers. In addition they received phone visits from a  
233 nurse to control for staff interaction and data collection.

234 Finally, the third RCT<sup>47</sup> evaluated the use of medical qigong compared with usual care to  
235 improve symptoms of fatigue, depression and quality of life of cancer patients. The  
236 intervention group consisted of two 90 minute medical qigong sessions per week for 10

237 weeks and participants were also encouraged to undertake home practice each day for 30  
238 minutes. The medical qigong programme was devised by an experienced, qualified medical  
239 qigong instructor and was modified by the instructor to specifically target the needs of cancer  
240 patients to control their emotions and stress as well as to improve their physical function.  
241 Each session included a 15 minute discussion of health issues, 30 minutes gentle stretching  
242 and body movement in standing postures, 15 minutes movement in seated positions and 30  
243 minutes meditation including breathing exercises, relaxation and visualisation. A self-report  
244 diary was used to document home practice. The control group received usual care, which was  
245 appropriate medical intervention. Control group participants were advised to undertake  
246 normal activities but refrain from joining an outside medical qigong class.

## 247 **Study Findings**

248 Table 2 provides a narrative summary of the effects of the exercise interventions on fatigue,  
249 dyspnoea and/or depression across the studies. Fatigue was reported on in nine studies<sup>41, 42,</sup>  
250<sup>44-50</sup>, dyspnoea in five studies<sup>42, 43, 48-50</sup> and depression in two studies<sup>47, 48</sup>.

### 251 **Fatigue**

252 Six<sup>42, 44-47, 49</sup> of the nine studies reporting on fatigue found statistically significant reductions  
253 in fatigue post-intervention. Three were RCTs<sup>42, 44, 47</sup> and three pre/ post-test studies<sup>45, 46, 49</sup>.  
254 Of the RCTs, one study<sup>42</sup> showed statistically significant improvements in fatigue in both the  
255 aerobic exercise (6±33%; p=0.009) and relaxation training groups (9±25%; p=0.02) at three  
256 weeks post interventions. The reduction of fatigue scores did not differ significantly between  
257 groups and there was no significant association between increase of maximal physical  
258 performance and reduction of fatigue scores. A second RCT<sup>44</sup> showed statistically significant  
259 improvements in fatigue in the exercise and balance programme group compared to the  
260 control group (p<0.001; 95% CI, -3.3 to -2.1, d=1.8) at six weeks post intervention. In

261 addition, the study found that fatigue was restored to lower than pre-surgery levels in the  
262 exercise and balance group ( $p>0.001$ ). The third RCT<sup>47</sup> found statistically significant  
263 improvements in fatigue in the medical qigong group compared to the control group (mean  
264 difference 5.70 (95% CI 3.32 to 8.09) at 10 weeks post intervention. Participants in medical  
265 qigong group also reported a clinically significant change in their levels of fatigue.

266 Of the three pre/post-test studies<sup>45, 46, 49</sup> one showed statistically significant improvements in  
267 fatigue at 12 weeks post the exercise intervention ( $p\leq 0.01$ ; mean difference 9.19 (6.18 –  
268 12.14, CI 95%); effect size 1.11)<sup>45</sup>. In addition 64% of participants reached the minimally  
269 important clinical difference for fatigue. The second study<sup>46</sup> showed statistically significant  
270 improvements in fatigue 14 weeks post intervention ( $p=0.03$ ; mean difference -7 (95% CI -1  
271 to -17)). It also found statistically significant improvements in fatigue post-intervention for  
272 participants who had not received chemotherapy ( $p=0.03$ , mean difference -10 (95%CI -18 to  
273 -2), whilst no statistically significant improvements in fatigue post-intervention were found in  
274 participants ( $p=0.62$ , mean difference -2 (95% CI -10 to 7) who had received chemotherapy.  
275 Finally, the third study<sup>49</sup> found statistically significant reductions in fatigue at four weeks  
276 post intervention ( $p<0.001$ ).

277 The remaining three studies<sup>41, 43, 50</sup> showed no statistically significant changes in fatigue pre  
278 or post intervention.

## 279 **Dyspnoea**

280 Of the five studies reporting on dyspnoea, two studies<sup>43, 49</sup> found statistically significant  
281 improvements in dyspnoea at four weeks post-intervention, compared to baseline. Glatki et  
282 al (2010) showed statistically significant improvements in dyspnoea post intervention (mean  
283 difference -0.26 +/- 0.61;  $p=0.007$ ) compared to baseline<sup>43</sup>; Riesenberget al (2017) also  
284 found statistically significant improvements in dyspnoea post intervention (mean difference -

285 13.7,  $p < 0.001$ ) compared to baseline<sup>49</sup>. Of the three remaining studies, one was an RCT and  
286 showed no statistically significant differences between aerobic exercise and relaxation  
287 training groups at three weeks post intervention<sup>42</sup>, whilst the two pre/post-test studies found  
288 no differences in dyspnoea at eight<sup>50</sup> and 10 weeks<sup>48</sup> post-intervention, compared to  
289 baseline.

## 290 **Depression**

291 Of the two studies reporting on depression, one was an RCT<sup>47</sup> and one a pre/post-test design  
292<sup>48</sup>. The RCT showed a statistically significant reduction in depression in the medical qigong  
293 group compared to the control group at 10 weeks post-intervention (mean difference -2.56  
294 (95% CI -5.14 to 0.01),  $p = 0.029$ <sup>47</sup>). The pre/post-test study found no statistically significant  
295 differences in depression pre ( $3.8 \pm 4.2$ ) or post ( $4.4 \pm 5.6$ ) intervention<sup>48</sup>. However, mean  
296 depression scores did move in a positive direction post intervention.

## 297 **Adverse Events**

298 One of the studies reported three adverse events relating to the exercise intervention; these  
299 were an exacerbation of shoulder arthritis, lower back pain and shoulder pain<sup>48</sup>. All were  
300 reported to successfully resolve.

301

## 302 **Discussion**

303 This review has examined the effects of exercise interventions on lung cancer survivors'  
304 fatigue, dyspnoea and depression levels. The findings suggest there is some evidence that  
305 exercise interventions can improve symptoms of fatigue, dyspnoea and depression in this  
306 population group. The interventions appear feasible and acceptable but more rigorous, larger  
307 scale RCT study designs are needed to determine their effectiveness. This would help identify

308 whether certain types of exercise interventions can be used to improve multiple symptoms  
309 simultaneously, or whether specific exercises are better targeted to specific symptoms.

310 Our review adds to existing systematic reviews in this area as it includes all studies reporting  
311 on any type of exercise intervention. In addition, it focuses on lung cancer survivors, a cancer  
312 group who are largely underrepresented in research studies, compares to other cancer types  
313 <sup>30</sup>. The review highlights the need for more robust research to be undertaken in this area to  
314 provide informed and credible information and facilitate improved outcomes for lung cancer  
315 survivors. Additionally, the review has focused on whether exercise specifically improves  
316 symptoms of fatigue, dyspnoea and depression in lung cancer survivors. All of these  
317 symptoms commonly feature in lung cancer survivors' day to day life and this review sheds  
318 light on potential exercise interventions and techniques that might help to alleviate some of  
319 these problems post treatment.

320 Many of the included studies showed statistically significant improvements in fatigue,  
321 dyspnoea and/or depression. These studies included a wide range of exercise interventions,  
322 with varying levels of intensity, in a number of different locations, over different lengths of  
323 time. Furthermore, one study <sup>42</sup> found that there was no significant association between an  
324 increase of maximal physical performance and reduction of fatigue scores. This suggests that  
325 there are a variety of different exercise interventions that may be beneficial to lung cancer  
326 survivors and that there is no 'one-size fits all' approach; instead customised exercise  
327 screening and treatment plans are required <sup>6</sup>. Lung cancer survivors who may feel over faced  
328 at the prospect of undertaking high levels of resistance training or aerobic exercise can be  
329 reassured that gentler exercises such as breathing techniques or medical qigong may also be  
330 effective ways of improving their symptom control. Similarly, those people who are keen to  
331 get back to their pre- cancer fitness levels can have confidence that by engaging in high levels

332 of physical activity they can achieve positive results and may improve their symptoms of  
333 fatigue, dyspnoea and/or depression in the process.

334 The lack of reporting of adverse events in the majority of the studies infers that, whilst there  
335 is mixed evidence as to the benefits of exercise in improving symptoms of fatigue, dyspnoea  
336 and depression in lung cancer survivors, undertaking exercise is unlikely to cause any  
337 sustained harm. This is important to note as some cancer survivors may be deterred from  
338 exercising post treatment due to fears they may do further damage to their already fragile  
339 bodies <sup>51</sup>. Thus, patients can be reassured that undertaking exercise post cancer is safe and is  
340 unlikely to cause any untoward, long-term health effects, something which has been verified  
341 in other literature on this topic <sup>15, 16</sup>. The low drop-out rate across the studies, also suggests  
342 that exercise, at all levels, is generally acceptable to lung cancer survivors and can be  
343 maintained and incorporated into their daily lives. This contrasts with a recent study <sup>52</sup> which  
344 found that a diagnosis of lung cancer was negatively associated with participating in physical  
345 activity programmes, although the study focused on people with metastatic disease. Lung  
346 cancer survivors may have different attitudes and abilities regarding undertaking exercise  
347 compared to those with more advanced disease.

348 The review has also identified that relaxation and mind-based therapies may serve as  
349 important adjuncts <sup>47</sup> or alternatives <sup>42</sup> to exercise based interventions for improving both  
350 depression and fatigue in lung cancer survivors. Previous research <sup>9</sup> has indicated that cancer  
351 survivors place value in both mind and body based practices as a way of providing  
352 symptomatic relief, relaxation and a sense of control over their cancer. This review adds  
353 credence to these findings and suggests that both mind and body based interventions, when  
354 used alone, or in conjunction with one another, can be effective ways of improving fatigue  
355 and depression in lung cancer survivors. Thus it is important to consider the use of exercise

356 alongside other supportive care interventions, such as mindfulness, meditation and other  
357 psychosocial therapies, for effective patient outcomes <sup>30</sup>.

358 Finally, one study <sup>46</sup> included in the review found statistically significant improvements in  
359 fatigue post-intervention in participants who had not received chemotherapy, but these  
360 improvements were not found among participants who had received chemotherapy. This  
361 indicates that that the gruelling impact of chemotherapy on the body <sup>53, 54</sup> may be hard for  
362 lung cancer survivors to recover from, as the intensity of cancer related fatigue experienced  
363 increases during this time <sup>6, 55</sup> and may, in addition, make exercise regimes difficult to adhere  
364 to <sup>30</sup>. Nurses should consider the treatment pathways of lung cancer survivors when assessing  
365 which exercise or mind-based therapies might be useful to them. It may be that patients who  
366 have undergone chemotherapy may require more specialist input and resources to help them  
367 manage their fatigue in the long term.

368

### 369 **Limitations of the review**

370 Whilst the researchers endeavoured to conduct a thorough, comprehensive and systematic  
371 review of the existing literature on this topic, it is possible that some relevant studies may not  
372 have been captured in the study selection and screening process due to the diversity of  
373 exercise interventions being examined and because fatigue, dyspnoea or depression may not  
374 have been identified as one of the main outcomes being measured in some studies. In  
375 addition, the review does not allow for a comparison between the different types of exercise  
376 interventions and their effectiveness in improving fatigue, dyspnoea and/or depression, due to  
377 the limited information provided.

378

379 **Conclusion**

380 This review has identified that exercise interventions may be effective, and are unlikely to  
381 cause harm, for lung cancer survivors who wish to improve their symptoms of fatigue,  
382 dyspnoea and depression. However, the quality of the evidence provided is limited and more  
383 rigorous study designs are required to explore this important area further in order to provide  
384 lung cancer survivors with useful advice and guidance about which exercise interventions  
385 may be the most beneficial to help them self-manage these symptoms in survivorship.

386 NICE <sup>56</sup> recommend that the opinions and experiences of lung cancer patients and carers  
387 should be collected to improve the delivery of lung cancer services. The findings from this  
388 review will be used to inform a larger scale focus group study with lung cancer patients,  
389 carers, nurses and other health professionals to explore which types of exercise and or/ mind-  
390 based interventions are useful in improving symptoms of fatigue, dyspnoea and depression in  
391 lung cancer survivors. This information will be used to develop a self-management app for  
392 lung cancer survivors that will be used to provide patient centred, customised and tailored  
393 exercise recommendations to improve their symptom control.

394

395 **Implications for Practice**

396 The review has highlighted the need for nurses to employ a patient focused approach when  
397 considering which types of exercise interventions might be suitable for lung cancer patients  
398 in survivorship. The ‘one-size fits all’ approach is inappropriate here; instead customised  
399 exercise screening and treatment plans are required to enable nurses to provide lung cancer  
400 survivors with tailor made, patient focused exercise activities that complement their lifestyle  
401 needs, interests, abilities and requirements. Psychological and mind-based therapies may also

402 be used alongside, or as an alternative to, exercise to improve symptom control for lung  
403 cancer survivors; this should be considered by nurses and other health professionals when  
404 providing survivorship advice and support to lung cancer patients. Nurses need to carry out  
405 holistic, individualised care plans to ensure comprehensive assessments are conducted and  
406 appropriate self-management recommendations are communicated to lung cancer survivors.

407

408

409

410

411

412

413

414

415

416

417

418

419

420

421

422 **References**

- 423 1. Osborn R, Demoncada A. Psychosocial Interventions for Depression, Anxiety and Quality of  
424 Life in Cancer Survivors: Meta-analyses. **Int'l Journal Psychiatry in Medicine**. 2006;36(1):13-  
425 34.
- 426 2. Cancer Research UK. Lung Cancer Statistics. **Cancer Research UK**. Available at:  
427 [http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-](http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer#heading-Zero)  
428 [type/lung-cancer#heading-Zero](http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer#heading-Zero), 2017.
- 429 3. Ferrell B, Hassey K. Quality of Life Among Long-Term Cancer Survivors. **Oncology**.  
430 1997;11(4):565-571.
- 431 4. CancerCare. Managing Side Effects. **CancerCare**. Available at:  
432 [https://www.lungcancer.org/find\\_information/publications/163-lung\\_cancer\\_101/271-](https://www.lungcancer.org/find_information/publications/163-lung_cancer_101/271-treatment_side_effects)  
433 [treatment\\_side\\_effects](https://www.lungcancer.org/find_information/publications/163-lung_cancer_101/271-treatment_side_effects), 2017.
- 434 5. McCall S. Management of Dyspnea in Cancer Patients. **University of Pennsylvania**. Available  
435 at: [https://www.oncolink.org/healthcare-professionals/o-pro-portal/articles-about-cancer-](https://www.oncolink.org/healthcare-professionals/o-pro-portal/articles-about-cancer-treatment-and-medications/management-of-dyspnea-in-cancer-patients)  
436 [treatment-and-medications/management-of-dyspnea-in-cancer-patients](https://www.oncolink.org/healthcare-professionals/o-pro-portal/articles-about-cancer-treatment-and-medications/management-of-dyspnea-in-cancer-patients), 2017.
- 437 6. Carnio S, Francesco Di Stefano R, Novello S. Fatigue in lung cancer patients: symptom burden  
438 and management of challenges. **Lung Cancer: Targets and Therapy**. 2016;7:73-82.
- 439 7. Taskila T, Lindbohm M. Factors Affecting Cancer Survivors' Employment and Work Ability.  
440 **Acta Oncol**. 2007;46(4):446-451.
- 441 8. Henshall C, Greenfield S, Gale N. Typologies for restructuring relationships in cancer  
442 survivorship: temporal changes in social support and engagement with self-management  
443 practices. **Cancer Nursing**. 2017.
- 444 9. Henshall C, Greenfield S, Gale N. The role of self-management practices as mechanisms for  
445 re-establishing normality in cancer survivors. **Qual Health Res**. 2016.
- 446 10. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Impact of dyspnea, pain, and  
447 fatigue on daily life activities in ambulatory patients with advanced lung cancer. **Journal of**  
448 **Pain and Symptom Management**. 2002;23(5):417-423.
- 449 11. Akin S, Can G, Aydiner A, Ozdilli K, Durna Z. Quality of life, symptom experience and distress  
450 of lung cancer patients undergoing chemotherapy. **European Journal of Oncology Nursing**.  
451 2010;14:400-409.
- 452 12. Dy S, Lorenz K, Naeim A, Sanati H, Walling A, Asch S. Evidence based recommendations for  
453 cancer fatigue, anorexia, depression, and dyspnea. **Journal of Clinical Oncology**.  
454 2008;26(23):3886-3895.
- 455 13. Smith E, Hann D, Ahles T, et al. Dyspnea, anxiety, body consciousness, and quality of life in  
456 patient with lung cancer. **Journal of Pain and Symptom Management**. 2001;21(4):323-329.
- 457 14. Hensch I, Bergman B, Gustafsson M, Gaston-Johansson F, Danielson E. The impact of  
458 symptoms, coping capacity, and social support on quality of life experience over time in  
459 patients with lung cancer. **Journal of Pain and Symptom Management**. 2007;34(4):370-379.
- 460 15. Schmitz K, Courneya K, Matthews C, et al. American College of Sports Medicine Roundtable  
461 on Exercise Guidelines for Cancer Survivors. **Medicine and science in sports and exercise**.  
462 2010:1409-1426.
- 463 16. Jones L, Eves N, Haykowsky M, Freedland S, Mackey J. Exercise intolerance in cancer and the  
464 role of exercise therapy to reverse dysfunction. **Lancet Oncology**. 2009;10:598-605.
- 465 17. Shneerson C, Taskila T, Holder R, et al. Patterns of self-management practices undertaken by  
466 cancer survivors: variations in demographic factors. **European Journal of Cancer Care**.  
467 2015;24(5):683-694.
- 468 18. Loh S-Y, Ong L, Ng L-L, Chew S-L, Lee S-Y, Boniface G. Qualitative Experiences of Breast  
469 Cancer Survivors on a Self-Management Intervention: 2 Year post-Intervention. **ASJCP**.  
470 2011;12:1489-1495.

- 471 19. Korstjens I, May A, van Weert E, Mesters I, Tan F, Ros Wea. Quality of Life After Self-  
472 Management Cancer Rehabilitation: A Randomised Controlled Trial Comparing Physical and  
473 Cognitive-Behavioural Training Versus Physical Training. **Psychosomatic Medicine**.  
474 2008;70:422-429.
- 475 20. Damush T, Perkins A, Miller K. The Implementation of an Oncologist Referred, Exercise Self-  
476 Management Program for Older Breast Cancer Survivors. **Psycho-Oncology**. 2006;15:884-  
477 890.
- 478 21. Speck R, Courneya K, Mâsse L, Duval S, Schmitz K. An Update of Controlled Physical Activity  
479 Trials in Cancer Survivors: A Systematic Review and Meta-Analysis. **Jour Can Surviv**.  
480 2010;4:87-100.
- 481 22. Cramp F, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults.  
482 **Cochrane Database of Systematic Reviews**. 2012;11(CD006145).
- 483 23. Paramanandam V, Dunn V. Exercise for the management of cancer-related fatigue in lung  
484 cancer: a systematic review. **Eur J Cancer Care**. 2015;24(1):4-14.
- 485 24. Denlinger C, Ligibel J, Are Mea. NCCN Clinical Practice Guidelines in Oncology: Survivorship.  
486 Available at: [http://www.nccn.org/professionals/physician\\_gls/f\\_guidelines.asp#supportive](http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#supportive),  
487 2015.
- 488 25. American Cancer Society. ACS guidelines for nutrition and physical activity for cancer  
489 prevention. Available at:  
490 <http://www.cancer.org/healthy/eathealthygetactive/csguidelineson>  
491 nutritionphysicalactivity-forcancerprevention/acsguidelines-on-nutrition-and-physical-  
492 activity-for-cancer prevention-summary, 2014.
- 493 26. Reyes-Gibby C, Swartz M, Yu X. Symptom clusters of pain, depressed mood and fatigue in  
494 lung cancer: assessing the role of cytokine genes. **Support Care Cancer**. 2013;21(11):3117-  
495 3125.
- 496 27. Kenny P, King M, Viney Rea. Quality of life and survival in the 2 years after surgery for non  
497 small-cell lung cancer. **J Clin Oncol**. 2008;26:233-241.
- 498 28. National Institute for Health and Care Excellence. Depression in adults with a chronic  
499 physical health problem: recognition and management. **National Institute for Health and  
500 Care Excellence**. Available at: [https://www.nice.org.uk/guidance/CG91/chapter/1-  
501 Guidance#step-1-recognition-assessment-and-initial-management-in-primary-care-and-  
502 general-hospital](https://www.nice.org.uk/guidance/CG91/chapter/1-Guidance#step-1-recognition-assessment-and-initial-management-in-primary-care-and-general-hospital), 2017.
- 503 29. Brown J, Huedo-Medina T, Pescatello L, Pescatello S, Ferrer R, Johnson B. Efficacy of Exercise  
504 Interventions in Modulating Cancer-Related Fatigue among Adult Cancer Survivors: A Meta-  
505 Analysis. **Cancer Epidemiol Biomarkers Prev**. 2011;20(1):123-133.
- 506 30. Courneya K. Physical activity in cancer survivors: a field in motion. **Psycho-Oncology**.  
507 2009;18:337-342.
- 508 31. Alberg A, Nonemaker J. Who is at high risk for lung cancer? Population-level and individual-  
509 level perspectives. **Semin Respir Crit Care Med**. 2008;29(3):223-232.
- 510 32. Rueda J, Sola I, Pascual A, Casacuberta M. Non-invasive interventions for improving  
511 wellbeing and quality of life in patients with lung cancer. **Cochrane Database of Systematic  
512 Reviews**. 2011;CD004282(9).
- 513 33. Cavalheri V, Tahirah F, Nonoyama M, Jenkins S, Hill K. Exercise training undertaken by  
514 people within 12 months of lung resection for non-small cell lung cancer (review). **Cochrane  
515 Database of Systematic Reviews**. 2013;CD009955(7).
- 516 34. Eldridge L. Lung Cancer and Depression. Depression vs Grief with Lung Cancer. Available at:  
517 <https://www.verywell.com/lung-cancer-and-depression-2249229>.
- 518 35. Coups E, Ostroff J, Feinstein Mea. Correlates of physical activity among lung cancer  
519 survivors. **Psycho-Oncology**. 2009;18:395-404.
- 520 36. Schwartz A. Patterns of exercise and fatigue in physically active cancer survivors. **Oncology  
521 Nursing Forum**. 1998;25(3):485-491.

- 522 37. Pope C, Mays N, Popay J. **Synthesizing qualitative and quantitative health evidence: a guide**  
523 **to methods**. Buckingham: Open University Press; 2007.
- 524 38. PRISMA. Transparent reporting of systematic reviews and meta-analyses. **University of**  
525 **Oxford**. Available at: <http://www.prisma-statement.org/>, 2017.
- 526 39. Winer E, Gralow J, Diller L, Karlan B, Loehrer P, Pierce Lea. Clinical Cancer Advances 2008:  
527 Major Research Advances in Cancer Treatment, Prevention, and Screening—A Report From  
528 the American Society of Clinical Oncology. **Journal of Clinical Oncology**. 2009;27(5):812-826.
- 529 40. CASP. Critical Appraisal Skills Programmes (CASP). Making Sense of Evidence. **CASP UK**.  
530 Available at: <http://www.casp-uk.net/>, 2017.
- 531 41. Christopher K, Morrow L. Evaluating a community based exercise program for women cancer  
532 survivors. **Applied Nursing Research**. 2004;17(2):100-108.
- 533 42. Dimeo F, Thomas F, Raabe-Menssen C, Propper F, Mathias M. Effect of exercise and  
534 relaxation training on fatigue and physical performance of cancer patients after surgery. A  
535 randomised controlled trial. **Support Care Cancer**. 2004;12:774-779.
- 536 43. Glattki G, Manika K, Sichletidis L, Alexe G, Brenke R, Spyrtos D. Pulmonary rehabilitation in  
537 non-small cell lung cancer patients after completion of treatment. **American Journal of**  
538 **Clinical Oncology**. 2012;35(2):12--125.
- 539 44. Hoffman A, Brintnall R, Given B, von Eye A, Jones L, Brown J. Using perceived self-efficacy to  
540 improve fatigue and fatigability in post-surgical lung cancer patients. **Cancer Nursing**.  
541 2017;40(1).
- 542 45. Janssen S, Abbink J, Lindeboom R, Vliet Vlieland T. Outcomes of pulmonary rehabilitation  
543 after treatment for non-small cell lung cancer stages I to IIIa. **Journal of Cardiopulmonary**  
544 **Rehabilitation and Prevention**. 2017;37:65-71.
- 545 46. Jones L, Eves N, Peterson B, et al. Safety and feasibility of aerobic training on  
546 cardiopulmonary function and quality of life in postsurgical nonsmall cell lung cancer  
547 patients. A pilot study. **Cancer Epidemiol Biomarkers Prev**. 2008;113(12):3430-3439.
- 548 47. Oh B, Butow P, Mullan B, et al. Impact of medical qigong on quality of life, fatigue, mood and  
549 inflammation in cancer patients: a randomised controlled trial. **Annals of Oncology**.  
550 2010;21:608=614.
- 551 48. Peddle-McIntyre C, Bell G, Fenton D, McCargar L, Courneya K. Feasibility and preliminary  
552 efficacy of progressive resistance exercise training in lung cancer survivors. **Lung Cancer**.  
553 2012;75:126-132.
- 554 49. Riesenbergh H, Lubbe A. In-patient rehabilitation of lung cancer patients - a prospective  
555 study. **Support Care Cancer**. 2010;18:877-882.
- 556 50. Spruit M, Janssen P, Willemsen S, Hochstenbag M, Wouters E. Exercise capacity before and  
557 after an 8 week multidisciplinary inpatient rehabilitation program in lung cancer patients: a  
558 pilot study. **Lung Cancer**. 2006;52:257-260.
- 559 51. Shneerson C. *Self-management strategies of cancer survivors: who does what and why? A*  
560 *mixed methods study*. Birmingham: Primary Care Clinical Sciences, Birmingham; 2014.
- 561 52. Lowe S, Danielson B, Beaumont C, Watanabe S, Courneya K. Physical activity interests and  
562 preferences of cancer patients with brain metastases: a cross-sectional survey. **BMC**  
563 **Palliative Care**. 2016;15(7).
- 564 53. Sitzia J, Hughes J, Sobrido L. A Study of Patients ' Experiences of Side-Effects Associated with  
565 Chemotherapy: Pilot Stage Report. **Int J Nurs Stud** 1995;32(6):580-600.
- 566 54. Shneerson C, Gale N. Using mixed methods to identify and answer clinically relevant  
567 research questions. **Qualitative Health Research**. 2015;25(6):845-856.
- 568 55. Maguire R, Papadopoulou C, Kotronoulas G, Simpson M, McPhelim J, Irvine L. A systematic  
569 review of supportive care needs of people living with lung cancer. **Eur J Oncol Nurs**.  
570 2013;17(4):449-464.

571 **56.** Excellence NfHaC. Lung Cancer: Diagnosis and Management. **National Institute for Health**  
572 **and Care Excellence,**. Available at: [https://www.nice.org.uk/guidance/cg121/chapter/1-](https://www.nice.org.uk/guidance/cg121/chapter/1-Guidance#palliative-interventions-and-supportive-and-palliative-care)  
573 [Guidance#palliative-interventions-and-supportive-and-palliative-care](https://www.nice.org.uk/guidance/cg121/chapter/1-Guidance#palliative-interventions-and-supportive-and-palliative-care), 2017.

574

575 **Figure Legends**

576 Figure 1: PRISMA flow diagram outlining search strategy for review

577