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Invited Topical Review

Physiotherapy management of lung cancer

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KEY WORDS

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Introduction

Lung cancer is associated with significant morbidity and mortality and is a substantial burden to healthcare systems. Physiotherapists play an important role in the management of people with lung cancer. Advances in research over the past decade, particularly supporting the use of exercise training, have rapidly progressed the role of physiotherapy in lung cancer. This review summarises the burden associated with lung cancer, the management of lung cancer with a particular focus on physiotherapy interventions, and future directions for research and clinical practice.

What is lung cancer?

Cancer is a generic term for a heterogeneous group of diseases that occur when abnormal cells are not destroyed by normal metabolic processes, but instead proliferate and metastasise out of control.[1] Lung cancer is the leading type of cancer diagnosed in males worldwide.[2] In females, lung cancer is the fourth most common cancer diagnosed behind breast cancer, colorectal cancer and cancer of the cervix uteri.[2] Multiple factors are understood to play a role in the induction of lung carcinogenesis. Tobacco smoking is the leading cause.[3] Other risk factors include exposure to environmental or occupational carcinogens, pulmonary inflammation, airflow limitation, chronic obstructive pulmonary disease (COPD) and genetic predisposition.[1,3,4] Weaker evidence links physical inactivity and poor nutrition to an increased risk of lung cancer.[5] Non-small cell lung cancer (NSCLC) is the most common type of lung cancer and accounts for 85% of new lung cancer diagnoses.[6] Small cell lung cancer accounts for a small proportion of lung cancer diagnoses and is remarkably different to NSCLC in terms of aetiology, prognosis and treatment.[6] This review mainly focuses on NSCLC, which is where the majority of physiotherapy research exists.

Lung cancer is a disease predominantly seen in the elderly population; more than 80% of people diagnosed with lung cancer are aged 60 years or older.[6] Due to the high incidence of smoking among people with lung cancer, multi-morbidities are common.[7] The most common of these is COPD, occurring in 40 to 70% of people with lung cancer.[3,4] Due to the aetiology of lung cancer, the older age of patients, and presence of multi-morbidities, people with lung cancer constitute a complex patient population to manage.

Medical management of lung cancer

The medical treatment of lung cancer has improved over recent decades; however, lung cancer remains the leading cause of cancer death worldwide and the overall 5-year survival rate is 14%.[2] Medical treatments include surgical resection, chemotherapy, radiotherapy and targeted agents, each of which is associated with several side effects (Box 1). The choice of treatment combination depends on the histological type, tumour location, cancer stage and the patient's degree of frailty.[8]

Surgical resection

Surgical resection of the tumour provides the best potential chance of cure; however, approximately 70% of people present with advanced inoperable disease and 25% of people with operable disease are unfit for surgery.[8] For those people who are able to undergo surgery, surgical options include pneumonectomy, lobectomy or sub-lobar resection.[9] Lobectomy is the preferred surgical approach over limited pulmonary resection in early stage NSCLC as it is associated with lower rates of loco-regional recurrence and improved survival.[9] However, limited pulmonary resection is advantageous in terms of preserving a greater amount of lung volume, limiting postoperative physiological impairment and, consequently, reducing postoperative complications and hospital length of stay.[9] Video-assisted thoracoscopic surgery is the preferred approached over a thoracotomy incision and is associated with: less pain, better shoulder range of motion and improved function early after surgery; fewer postoperative complications; decreased risk of intensive care readmission; shorter hospital length of stay; and less need for inpatient rehabilitation.[8,10,11] Following lung resection, clinically important

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Box 1. Common side effects resulting from lung cancer treatments.

Surgery	Chemotherapy	Radiotherapy	Molecular targeted therapies
• pain • cough • fatigue	• fatigue • nausea • infection • vomiting • anaemia • diarrhoea • constipation • loss of appetite • hair loss • mouth ulcers • weight gain or loss	• fatigue • cough • oesophagitis • nausea • vomiting • skin erythema • diarrhoea • loss of appetite • hair loss • rigors • flu-like symptoms	• fatigue • nausea • vomiting • loss of appetite • diarrhoea • constipation • skin and hair changes

immediate postoperative pulmonary complications (PPCs) can include respiratory failure (prolonged mechanical ventilation, re-intubation or acute respiratory distress syndrome), pneumonia and atelectasis requiring bronchoscopy.[12] Reported rates of PPCs vary from 3 to 15%; this is partly due to a lack of consensus on a PPC definition.[13,14] Postoperative pulmonary complications are associated with increased hospital length of stay, intensive care readmissions and mortality.[13]

Chemotherapy

Chemotherapeutic agents inhibit cell division in both cancerous and non-cancerous cells and therefore result in side effects due to the damage caused to normal cells.[15] These side effects include bone marrow suppression and resultant immunosuppression, which are worst 2 weeks following treatment,[16] and impaired respiratory function, particularly diffusing capacity.[17]

Radiotherapy

External beam radiotherapy works by producing radiation, which is targeted at the tumour, and results in apoptosis of the cancerous cells. Side effects of radiotherapy occur due to the associated formation of free radicals, widespread inflammatory response and release of cytokines.[15] Respiratory function, particularly diffusing capacity, is impaired following radiotherapy.[18]

Molecular-targeted agents

Tumours are driven by genomic mutations and, increasingly, the different genomes in NSCLC are being recognised and targeted in the treatment of the disease. Targeted agents differ from chemotherapy agents because they inhibit 'pathways outside of the nucleus that are required for malignant proliferation chemotherapy agents to act', whereas chemotherapy agents act in the nucleus by inhibiting the division of any rapidly dividing cells.[19]

In summary, lung cancer is associated with adverse physiological impairments that arise from multiple causative factors, including: the disease, treatment, multi-morbidities and pre-existing harmful lifestyle behaviours. Consequently, this leads to significant disease burden.

Burden of lung cancer

Lung cancer is associated with higher disease burden, more physical hardship and greater symptom distress than other cancer types.[6,20,21] Important symptoms include dyspnoea, fatigue, cough, pain and insomnia. These often occur as symptom clusters and result in high patient distress and interference with daily activities.[21,22] Distress due to symptoms at the time of diagnosis is predictive of mortality.[20] Avoidance of symptom triggers (namely physical activity) promotes a vicious cycle of inactivity and functional decline; a phenomenon that is becoming well described in the lung cancer literature and a cycle that is important for physiotherapists to address.[23]

Cancer cachexia is a multi-factorial syndrome defined by an ongoing loss of skeletal muscle mass that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment.[24] Clinically, cancer cachexia presents as a combination of anorexia, metabolic alterations, loss of fat mass, loss of skeletal muscle protein, loss of weight, impaired muscle strength and fatigue.[24] Important implications include reduced ability to tolerate surgery, poor response to chemotherapy or radiotherapy, impaired resilience to treatment, worse health-related quality of life and increased mortality.[24] At diagnosis, people with lung cancer have reduced peripheral muscle strength compared to healthy aged-matched peers.[23] Skeletal muscle dysfunction is likely to significantly contribute to exercise intolerance, particularly given that 70% of preoperative peak exercise tests are stopped due to leg discomfort rather than dyspnoea, and functional capacity is not related to spirometric measures of lung function in this population.[25,26] Peripheral muscle strength declines further during and after lung cancer treatment.[23] Given the importance of peripheral muscle strength to overall physical function, this impairment is an important feature of lung cancer for physiotherapists to manage.

Following diagnosis, functional decline is common and rapid, and activity limitations and participation restrictions commonly ensue.[23,27,28] At diagnosis, functional capacity is reduced compared to healthy aged-matched peers.[23] Functional capacity measured preoperatively is predictive of postoperative outcomes, including: respiratory failure, hospital length of stay, health-related quality of life and survival.[29] Functional capacity is also predictive of survival in advanced lung cancer. With every 50 m improvement in the 6-minute walk test, survival improves by 13% and people who walk at least 400 m before chemotherapy have greater survival time.[30,31] A number of studies have reported that functional capacity progressively declines after diagnosis; however, it is possible that this decline may be limited to the inoperable population. In the surgical literature, most studies report functional capacity to temporarily decline after lung resection and then return to baseline by 3 to 6 months postoperatively.[32,33] Conversely, people undergoing a pneumonectomy experience sustained reductions in functional capacity postoperatively.[33] Deterioration in functional capacity is also observed during chemotherapy. An Australian study, including people with operable and inoperable lung cancer, found an overall large clinically and statistically significant mean decline of 78 m in the 6-minute walk test over 6 months from diagnosis, suggesting that in many people, functional capacity does not recover back to pre-treatment levels in the short term.[23] Not surprisingly, functional capacity is the most common endpoint targeted by lung cancer exercise trials to date.[29]

Physical inactivity is common and prevalent in lung cancer. Studies have demonstrated that before surgery or treatment, physical activity levels are low and less than those of healthy aged-matched peers; this is based on self-report and objective measures.[23,34,35] United States and Australian data show that only 26% and 40% of people with lung cancer meet cancer-specific recommended physical activity levels, respectively.[23,34] Importantly, before treatment, higher physical activity levels are seen in people with better functional capacity, muscle strength, physical function, nutritional status and self-determination to exercise, and less anxiety, depression, distress, fatigue and symptoms.[23,35] There are many reasons why people with lung cancer may be inactive at diagnosis: they might have been inactive for a large proportion of their life (this is a risk factor for developing cancer) or physical activity levels may have already declined as the cancer progressed prior to detection; the latter is more likely in the inoperable (more advanced cancer) group. The cancer cachexia process starts early and many of the features can progress significantly before diagnosis.[24] Following surgery and treatment, physical activity levels decline further. Agostini and colleagues[36] found very low levels of physical activity immediately postoperatively during the inpatient stay (3% of preoperative steps/day); and Novoa and colleagues[37] found 25% and 49% reductions in steps per day compared to preoperative values 30 days after lobectomy and pneumonectomy, respectively. During cancer treatment, only 26% of people meet the recommended activity levels[27] and higher physical activity levels are seen in people with better physical function and health-related quality of life, and with lower symptoms and depression.[23] Importantly, it is unknown if this is a causal relationship. It is possible that people are able to be more active because they have fewer symptoms and better health-related quality of life; conversely, being active can reduce symptoms (or desensitise the person to the symptoms) and enhance quality of life.[38] Six months after diagnosis, physical activity levels remain reduced, with only 31% of survivors meeting the recommendations.[23] Survivors of lung cancer have long-term reductions in physical activity and health-related quality of life, and even experience fatigue 5 years following surgery.[39,40]

In summary, the physical and psychological implications of lung cancer are severe, disabling and long-standing. They have significant ramifications for the patient, the family/carers and the healthcare system. Physiotherapy management is important to address these issues in lung cancer.

Physiotherapy management of lung cancer

A summary of the physiotherapy interventions that are used in the management of lung cancer, along with the level of evidence that underpins their use, is provided in Figure 1. Physiotherapy interventions vary depending on the stage in disease trajectory and timing relative to treatment. Physiotherapy services for lung cancer have historically been hospital-based and focused on PPCs after surgery.[41] Other physiotherapy interventions, such as exercise training, are less frequently performed as routine clinical practice, despite the rapid growth of evidence supporting these interventions over the last decade.

The cornerstone of physiotherapy management in lung cancer should be prescription and delivery of exercise intervention. Physical activity and exercise are vital components targeting three main aspects of the cancer continuum: prevention, mortality and morbidity. The American Cancer Society recommends that adults with cancer engage in at least 150 minutes of moderate-intensity aerobic exercise and two sessions of resistance exercise per week, which is the same as the guidelines for the general adult population.[42,43] These recommendations are supported by strong evidence derived predominantly from other cancer populations. Higher physical activity levels are protective against developing colon, pancreatic, endometrial and prostate cancer.[42] Excessive sedentary time, independent of moderate and vigorous physical activity, is associated with increased risk of developing cancer.[44] Higher physical activity levels after cancer diagnosis are associated with reduced cancer-specific and all-cause mortality in breast, colon and prostate cancer.[45,46] Additionally, there is emerging evidence linking post-diagnosis sedentary time with reduced cancer-specific mortality as well.[44] It is important to note that the evidence, to date, in the general cancer population is limited by lack of prospective research designs, longitudinal repeated measurement of physical activity and control for other important prognostic factors. The mechanisms between these associations are not well understood. It is hypothesised that exercise modulates circulating metabolic and sex-steroid hormone concentrations, immune surveillance, and reduces systemic inflammation/oxidative damage.[47] In lung cancer specifically, there are only a small number of studies investigating the link between physical activity and development of lung cancer, and they report conflicting results. There is a strong rationale for more research to be conducted in this area, given the high potential clinical significance of physiotherapy and exercise to target lung cancer prevention and survival as outcomes.

There is growing evidence for exercise interventions to reduce cancer morbidity in lung cancer. The role of exercise in this situation is to prevent deterioration and to maximise or restore physical status prior to, during and following treatment. A previous Cochrane review and three systematic reviews have been conducted in the area of lung cancer specifically.[48–51] The majority of research, to date, has been performed in the preoperative or postoperative treatment stage of lung cancer, with a smaller number of studies investigating the role of exercise during treatment or in advanced disease. The evidence supporting exercise at these different time points is summarised in subsequent sections.

Prehabilitation

Prehabilitation is exercise delivered prior to surgery or treatment. There are two clinical rationales for this. Prehabilitation can be used for: operable patients (assessed to be fit for surgery) to maximise their physical status prior to the insult of surgery and reduce postoperative morbidity; or inoperable patients (deemed unfit for surgery based on cardiovascular impairment) to improve their physical status enough for them to become operable. The evidence supporting prehabilitation is still in its infancy. Most of the research to date has been conducted in patients already deemed operable and, generally, studies are small and limited by lack of randomisation and/or control groups. Prehabilitation is not yet part of routine clinical practice worldwide. Until further research suggests otherwise, in already operable patients, it is currently not recommended to delay surgery in order to undertake prehabilitation, but rather use the time waiting for surgery opportunistically to deliver prehabilitation as able.

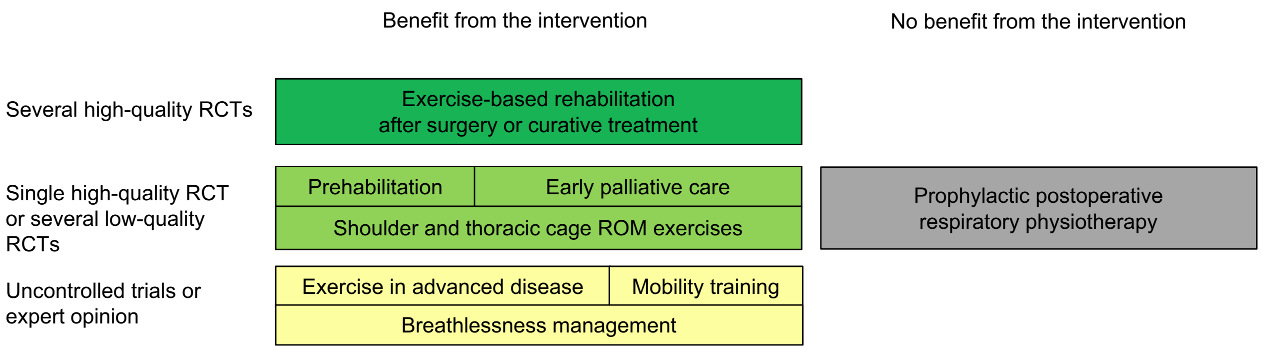

Figure 1. Interventions for the management of lung cancer with associated levels of evidence.
ROM = range of motion, RCT = randomised, controlled trial.

The three systematic reviews in this area include a small number of studies and an even smaller number of randomised, controlled trials. There are nine studies inclusive of five randomised trials delivering exercise preoperatively and two studies inclusive of one randomised trial delivering exercise both preoperatively and postoperatively.[48,49,51] To date, meta-analyses have not been conducted due to lack of robust trials and heterogeneity of measures and interventions.[48,49,51] One randomised trial was stopped early due to poor recruitment (n = 9);[52] three other randomised trials reported that prehabilitation was associated with reduced hospital length of stay,[53,54] PPCs,[53,54] and/or days needing a chest tube postoperatively,[52] as well as improved respiratory function immediately post intervention.[53,54] One randomised trial [52] found conflicting results (no effect for hospital length of stay or PPCs between groups) and currently the evidence is not definitive. The systematic reviews, inclusive of the evidence from non-randomised trials (mostly single-group studies), demonstrate that people who undergo prehabilitation experience improved functional capacity immediately after intervention.[48,49,51] There is limited research regarding the impact of prehabilitation for inoperable patients and only one article included in the systematic reviews addressed this: Fang and colleagues[55] included both participants who were deemed operable and inoperable. Notably, their results demonstrated that 59% (n = 10/17) of the inoperable group were re-classified as operable after exercise training and postoperatively there was no statistical difference in PPC rate between the (initially) operable group (34%) and (initially) inoperable group (40%). Since the systematic reviews, one further randomised trial has been published,[56] as well as seven more non-randomised trials (mostly single-group studies), which confirm the previous findings. The interventions tested in studies to date were predominantly individual, supervised, outpatient-based and delivered five times a week for a median of 4 weeks (range: 1 to 10 weeks). All studies included aerobic exercise training and over half also included resistance training. Whilst the evidence suggests that prehabilitation is safe, questions remain regarding the feasibility. Generally, the time between lung cancer diagnosis and surgery is short (< 1 month). Whilst some studies have shown successful effects of short-term exercise training, the challenge exists in both clinical and research settings to recruit, assess and commence exercise as soon as possible after diagnosis, to maximise the length of time available for exercise training. This issue may challenge the translation of evidence supporting prehabilitation into clinical practice.

In summary: the evidence supporting prehabilitation in lung cancer is emerging, particularly for people already deemed fit for surgery. The small number of randomised trials conducted to date provide preliminary evidence that prehabilitation may be beneficial in improving postoperative outcomes such as reduced hospital length of stay and PPCs. The evidence in this area is limited by lack of randomised trials and further work is required before prehabilitation should be translated into routine clinical practice for people undergoing surgery for lung cancer.

Perioperative management

Physiotherapy management in the immediate postoperative period aims to treat PPCs, prevent musculoskeletal sequelae, and facilitate early and safe discharge home. Hospital length of stay after lung resection is generally short (5 to 6 days), although length of stay is longer for patients who develop a PPC.[14] Physiotherapy principles include early mobilisation commenced on the first postoperative day, sitting out of bed and supported coughing. Shoulder/thoracic cage exercises are prescribed after removal of the intercostal catheter and are associated with reduced pain and improved function in the short term.[14,57]

There is a lack of evidence to support to use of prophylactic targeted respiratory physiotherapy interventions for routine patients managed on a clinical pathway following lung resection.[51] Physiotherapy management of this cohort has changed over the last decade due to improvements in pain management and the increasing use of video-assisted thoracic surgery and clinical pathways. Thoracic surgery clinical pathways incorporate physiotherapy principles and early mobilisation in daily nursing care and are associated with reduced hospital length of stay (Box 2).[58] The landmark randomised trial by Reeve and colleagues[14] demonstrated no difference in PPC rate or hospital length of stay for participants treated with prophylactic targeted respiratory physiotherapy (deep breathing and coughing, mobilisation, progressive shoulder/thoracic mobility exercises) plus usual care, compared to usual care alone (no physiotherapy). Usual care included a clinical pathway with early mobilisation. The PPC rate was low at 3.9% and hospital length of stay was short at a median of 6 days.[14] Whilst this study is from a single centre in New Zealand and practice may differ in other countries, it is the most definitive study conducted to date and the only randomised trial in this area with a 'no physiotherapy' control group.[51] A number of other studies have demonstrated that there is no added benefit of adjuncts to physiotherapy (incentive spirometry, intermittent positive pressure breathing, flutter, positive pressure devices, or breathing and coughing exercises) on PPCs or length of stay.[51] Therefore, for hospitals using clinical pathways, physiotherapy services should be focused on assessment (with or without mobilisation) of thoracotomy patients on the first postoperative day and ongoing respiratory physiotherapy for high-risk patients or those who fall off the clinical pathway (ie, do not achieve set pathway goals or develop a PPC) (Box 2). Currently, there is no gold standard risk-prediction tool with which to identify high-risk patients or those who will develop a PPC; however, the known independent risk factors for PPC are being aged $\geq$ 75 years, having a body mass index $\geq$ 30 kg/m^2, an Anesthesiologists score $\geq$ 3, a current smoking history and COPD.[13] Independent factors predictive of lower postoperative physical activity are being aged $\geq$ 75 years, having a

Box 2. Example clinical pathway for patients after thoracotomy.[59]

Day 1 postoperative
- Sit out of bed in ward chair
- Ambulate $\geq$ 20 m on ward
  - $\pm$ portable supplemental oxygen if required to keep $SpO_2 \geq$ 95%
  - $\pm$ portable suction if large air leak present
  - $\pm$ assistance from one person if required
  - $\pm$ gait aid if patient is unable to ambulate despite assistance from one person
- Teach supported cough with towel wrap
- Commence respiratory physiotherapy if indicated (high-risk patient or presence of PPC)

Day 2 postoperative
- Ambulate $\geq$ 50 m on ward
  - $\pm$ portable supplemental oxygen if required to keep $SpO_2 \geq$ 95%
  - $\pm$ portable suction if large air leak present
  - $\pm$ assistance from one person if required
  - $\pm$ gait aid if patient unable to ambulate despite assistance from one person
- Encourage supported cough
- Commence or continue respiratory physiotherapy if indicated (high risk or presence of PPC)

Day 3+ postoperative
- Review by physiotherapist only if patient requires ongoing mobility assistance or respiratory physiotherapy

Once intercostal catheters are removed
- Teach upper limb and thoracic mobility range of motion exercises
- Physiotherapy completes a discharge mobility assessment and provides any discharge planning as required for safety

predicted forced expiratory volume in one second (FEV_1) < 70% and lower self-reported preoperative physical activity;[36] this suggests that these patients may be the ones to not meet clinical pathway goals. Physiotherapy interventions used to treat PPCs related to low lung volumes or sputum production/retention include additional mobilisation, thoracic expansion exercises, sustained maximal inspirations, active cycle of breathing techniques and continuous positive airway pressure.

Physiotherapists are involved in the assessment of patients' safety related to mobility for hospital discharge. Most patients following lung resection are able to be discharged directly home; however, a small proportion of patients (2% in an Australian study)[59] do not regain a satisfactory degree of independence required for their social situation and home environment. These patients can be transferred to a sub-acute inpatient rehabilitation facility for a period of intensive physiotherapy/rehabilitation targeting function and mobility.

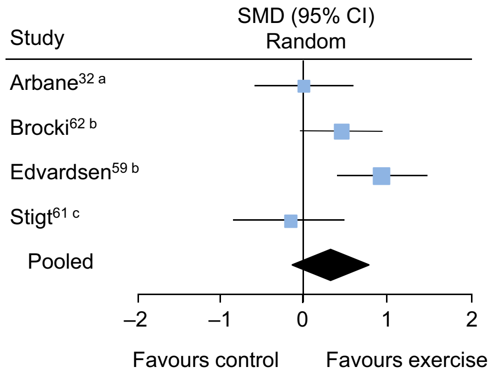

Figure 2. Effect of exercise after lung resection on health-related quality of life.
[a] Global function of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core 30.
[b] Physical component of the Medical Outcomes Study Short Form 36 General Health Survey.
[c] Total score of the St George's Respiratory Questionnaire.

Exercise following treatment

Exercise following surgery or treatment aims to restore physical status (addressing loss of functional capacity and muscle strength, which may occur during treatment) and to maximise function, physical activity, psychological status and health-related quality of life in the long term. The Cochrane review of exercise training after lung resection included three randomised trials involving 178 participants; it found significant improvements in functional capacity in favour of the intervention group (MD 50 m on the 6-minute walk test, 95% CI 15 to 85).[50] A large number of single-group studies have confirmed this finding and demonstrated reduced symptoms immediately after the intervention.[48–51] Since the Cochrane review there has been another randomised trial published;[60] this trial investigated the benefit of high-intensity aerobic and resistance training in people 5 to 7 weeks following surgery and similarly found improvements in functional capacity (peak oxygen uptake) in favour of the intervention group.[60] The Cochrane review of post-lung resection exercise on the outcomes of health-related quality of life and FEV_1 was inconclusive.[50,61,62] The addition of the subsequently published trial[60] to the meta-analysis continues to show no significant between-group difference for health-related quality of life (SMD 0.34, 95% CI –0.14 to 0.81) (Figure 2; see Figure 3 on the eAddenda for the detailed forest plot). Exercise following treatment with curative intent has also been researched in two randomised trials[63,64] and a number of single-group studies.[48,63] Exercise in this situation is also associated with improvements in functional capacity but not health-related quality of life.[48] Improvements in muscle strength are observed in people who undergo resistance training.[48] Exercise is also associated with reduced cancer symptoms, anxiety and depression.[48,63]

The interventions examined in studies to date are generally derived from the COPD and pulmonary rehabilitation literature, which has been extensively tested and implemented into clinical practice.[65] Hence, the majority of studies include both aerobic (ground walking, treadmill and/or stationary cycle) and resistance training components and, currently, this combined training approach is recommended. The addition of other components such as breathing exercises, dyspnoea management, balance exercises and stretches are used occasionally; however, the independent contribution of these training components to the resultant outcomes is unknown.[48–51] The randomised trial by Salhi and colleagues investigated the impact of whole body vibration training as an alternative to resistance training.[64] Results demonstrated significant improvements in functional capacity and quadriceps muscle strength in the resistance training group; however, this was not seen in either the whole body vibration training group or control group, suggesting that whole body vibration training is not an alternative to resistance training.[64] Generally, exercise programs are supervised, run for 8 to 12 weeks (range 4 to 14 weeks) and occur in an outpatient setting, although inpatient and home-based programs have also been used.[48–51] The exercise program should be individually tailored to the patient and there are a number of factors to consider when prescribing exercise for this population (Table 1).[66] Careful pre-exercise screening and

Table 1
General contraindications and precautions to exercise training.

Exercise	Patient cohort	Details
All	All	Avoid exercise if: • haemoglobin level < 80 g/l • neutrophil count ≤ 0.5 x 10^9/microlitre • platelet count < 50 x 10^9/microlitre • fever > 38 °C • extreme fatigue or severe nausea
	Upper or lower limb lymphoedema	Wear compression garment during exercise
Aerobic	Peripheral limitation such as severe cancer cachexia or muscle atrophy	Commence with resistance training and then progress to incorporate aerobic training once muscle bulk and strength is improved
Resistance	Known or high risk for bony metastases	Prescribe with caution (recommend medical clearance before commencement particularly for unstable bone or spinal metastases/fractures)
	High risk for osteoporosis	Prescribe with caution
	High risk for bone fracture	Prescribe with caution
	Cardiorespiratory limitation such as chemotherapy-induced left ventricular dysfunction or severe anaemia	Generally contra-indicated (recommend medical clearance before commencement)
	Postoperative patients	Care with wound healing – often requires 6 to 8 weeks postoperatively for healing prior to commencement of resistance exercises (recommend medical clearance before commencement)
Stretches	Postoperative patients	Avoid upper-limb stretches until removal of intercostal catheter

assessment, and monitoring throughout the exercise program is advised;[66] this includes consideration of the patient's co-morbidities. Tai Chi has been tested as an alternative form of exercise training;[67,68] a randomised trial involving patients following lung resection found a 16-week Tai Chi program to be associated with improved blood immune function.[67,68]

In summary, growing evidence suggests that exercise following surgery/treatment is associated with improvements in physical and physiological outcomes. Exercise in this setting is not yet routine clinical practice. In Australia and New Zealand, < 25% of patients are referred to pulmonary rehabilitation after lung resection.[41] Further randomised trials to strengthen the meta-analyses conducted to date will assist in the translation of evidence into routine clinical practice.

Exercise in advanced disease

Exercise for people with advanced lung cancer aims to prevent deterioration in physical and psychological status and maximise independence. This is an area that is currently being actively investigated. Several randomised trials are in progress in Australia, Denmark, Germany, Belgium and Spain, and they will significantly add to the body of literature in the near future.[69–72] The preliminary data from two randomised trials[73,74] and five non-randomised trials (mostly single-group studies)[75–79] published to date are promising. The randomised trial by Henke and colleagues demonstrated significant differences in favour of the intervention group for functional capacity, physical function, muscle strength, symptoms and health-related quality of life, despite 63% of the participants completing the trial (n = 29/46).[73] Results from some of the other studies have confirmed these findings and demonstrated improvements in functional capacity and muscle strength in study completers. The exception to this are the studies by Temel and colleagues[78] and Jastrzębski and colleagues,[79] which found no statistically significant change in these outcomes; although given the rapid functional decline that occurs in advanced lung cancer, maintenance is a positive result. Consistently, studies report no change in global health-related quality of life.[75–77] All studies included patients during treatment. One randomised trial investigated the benefit of exercise during targeted therapy and demonstrated that exercise was safe and associated with improved functional capacity, dyspnoea and fatigue.[74] The exercise programs tested were combined aerobic and resistance exercise delivered in either outpatient,[74,75,78] inpatient,[73,79] or both in-patient and outpatient settings.[76,77] Neuromuscular electrical stimulation may be an option for patients with severe symptoms that limit exercise performance, although a recent randomised trial demonstrated poor feasibility and no benefit when administered during palliative chemotherapy.[80] Unfortunately, study completion rates in the studies published to date are poor and range from 44 to 77%.[75–78] Research involving people with advanced lung cancer is particularly challenging, given the progressive nature of disease and short survival time following diagnosis. A proportion of non-completion in these studies is due to deaths.

Adherence to exercise training is an important issue in advanced lung cancer. Adherence rates vary greatly. Adherence to the exercise training sessions is higher for supervised hospital-based training (inpatient setting 95%,[76] outpatient setting 44 to 77%)[75–78] than for unsupervised home training (9%).[77] However, these adherence rates are from a small number of pilot studies and home-based training has not been tested in isolation. Home-based training is a highly appealing option. People with lung cancer are already required to attend the hospital frequently for appointments, investigations and treatment, and therefore the ability to deliver physiotherapy/exercise treatment away from the hospital is important. Home-based training also allows increased access for people living in rural areas and those without the ability to commute to the hospital. Telerehabilitation also poses a potential alternative model of delivery, where patients exercise at home whilst being monitored and supervised by health professionals located elsewhere.[81,82] Whilst the efficacy of telerehabilitation has not been investigated in lung cancer,[48] recently, Hoffman and colleagues reported that seven patients with lung cancer successfully used a movement-sensing gaming console[a] at home to complete walking and balance exercises.[83] Further research should investigate whether home-based exercise training is effective in advanced lung cancer and methods to promote adherence to unsupervised exercise.

Physiotherapy involvement in palliative care

Early palliative care is important in advanced lung cancer. A landmark study published in 2010 examined early palliative care consisting of: structured meetings with palliative care clinicians discussing physical and psychosocial symptoms; goals; decisions about treatment; and coordination of care. Compared with aggressive end-of-life care, this early palliative care improved survival, health-related quality of life and mood for people with metastatic lung cancer.[84] Physiotherapy management of this population includes management of breathlessness with breathing retraining, relaxation techniques and activity pacing. In an uncontrolled study, this was associated with improved breathlessness, functional capacity, physical activity levels and health-related quality of life, and less distress.[85] Commonly, patients are admitted to hospital with significant functional decline (to a point where the patient or carer cannot manage at home), or to a hospital/hospice in the end-of-life period for palliation. At this point in the disease trajectory, the focus of physiotherapy is on maximising the patient's physical independence and should be driven by his/her own goals and wishes. Physiotherapy interventions include assistance with mobilisation, provision of gait aids, and function-directed exercises such as sit-to-stand practice to optimise daily physical functioning.

Future directions for research and practice

The landscape of cancer research and treatment has changed significantly over the past two centuries. Commencing as an incurable disease with rising incidence and mortality rates, research and healthcare now allow cancer to be a curable disease for many, with mortality rates declining and a rise in the number of people living as cancer survivors in our communities. Unfortunately, the picture for lung cancer specifically is remarkably less favourable, and despite slight advances in medical treatment, survival rates remain dreadful. Research is urgently needed to address the efficacy of new treatments to improve the chance of cure in lung cancer. In 2005, the first paper was published showing that exercise improved survival in people with breast cancer.[86] Exercise has the potential to influence inflammation, tumour morphology, tumour growth and cancer recurrence.[87,88] The question of whether exercise improves survival in lung cancer is important and remains unanswered. The challenge over the next few decades is to test and establish the potential role that exercise may play in treating lung cancer with the ultimate aim of improving survival.

There are a number of limitations and gaps in the current literature. The exercise studies are generally small, lack randomisation and control groups, and rarely include long-term follow-up. The interventions tested vary in terms of timing, exercise type, duration and delivery. There is an abundance of studies in progress that seek to address these questions (55 open studies on ClinicalTrials.gov). Exercise in lung cancer is a growing area of practice and has the potential to minimise the debilitating physical and psychological decline that often occurs with lung cancer. As evidence emerges, an important target for physiotherapy over the next decade will be to rapidly translate findings of research studies into clinical physiotherapy practice.

Footnotes: [a]Nintendo Wii Fit plus, Nintendo Co, Ltd, Kyoto, Japan.

eAddenda: Figure 3 can be found online at doi:10.1016/j.jphys.2016.02.010

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