

A concise evidence review

Acknowledgements

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Executive summary

There is a growing evidence base indicating that physical activity has potential value at all stages of the cancer care pathway.

Preliminary evidence suggests that following an exercise programme before treatment (prehabilitation) leads to increased cardiorespiratory fitness, fewer post-operative complications and shorter hospital admissions.

There is stronger evidence demonstrating that exercising while undergoing cancer treatment helps to preserve cardiorespiratory and muscular fitness, and to control cancer-related fatigue.

Similarly, promising evidence indicates that after completion of treatment, undertaking an exercise programme leads to increased cardiorespiratory and muscular fitness, reduced fatigue, and improved body composition and wellbeing outcomes.

For patients under palliative care, preliminary evidence suggests that exercise is feasible, and may help maintain physical function, control fatigue, and improve bone health.

In addition, there is preliminary evidence that regular physical activity after a cancer diagnosis is associated with longer survival and lower risk of recurrence or disease progression. International guidelines recommend minimising inactivity at all times, maintaining some physical activity while undergoing treatment, and building towards age-appropriate guidelines for health-enhancing physical activity after completing treatment.

Key safety precautions include the avoidance of high-intensity activities when immunosuppressed, or experiencing pain, severe fatigue, or compromised bone health, and avoiding activities requiring balance when frail or experiencing dizziness or peripheral sensory neuropathy. In addition, anyone with a stoma should start with low resistance exercise and progress slowly to avoid herniation.

Background

Improved cancer survival rates, along with a growing and aging population, are contributing to increasing cancer prevalence. By 2040 it is estimated that a total of 5.3 million adults in the United Kingdom will be living with or beyond a cancer diagnosis, representing 6.2% of the male population and 8.5% of the female population.¹

Recognition of the importance of physical activity for people affected by cancer has expanded in recent years, and the evidence base is growing. Physical activity has potential benefit at all stages of the cancer care pathway (Figure 1), and this report provides a concise summary of the current research for adult populations. In addition, many cancer patients have comorbidities, with the most common being cardiovascular, metabolic, musculoskeletal and psychological disorders.² Physical activity has a role in the prevention and management of these conditions, thereby strengthening the need for greater focus on helping those affected by cancer to maintain healthy active lifestyles.

Healthcare professionals are well placed to promote physical activity with their patients. Studies have demonstrated that patients are receptive to advice about lifestyle factors, particularly soon after diagnosis,³ with even brief conversations effective in changing attitudes and behaviour.^{4,5}



Methods

This report replaces the Macmillan concise evidence review from 2011.⁶ The evidence presented here is based on the results of a longer report⁷ that summarises the findings of two comprehensive reviews of published systematic reviews of lifestyle factors for cancer outcomes.^{8,9} These reviews used rigorous approaches to locate, appraise, and grade evidence as high, moderate, low, or very low quality.

For the current report, the evidence base was updated to include any additional systematic reviews and high quality studies (randomised controlled trials [RCT] or prospective cohort studies) from 2010–2016 identified by searching the Cochrane Database of Systematic Reviews and two scientific databases specialising in medicine (MEDLINE), and physical activity (SPORTDiscus). The original evidence gradings were renamed as compelling, promising, and preliminary for the current report to provide a simple representation of the quality, strength, and consistency of the body of evidence available for the outcomes presented (Figure 2).

Compelling

High quality body of evidence with no uncertainty over the effects demonstrated.

Promising

Moderate quality body of evidence with some uncertainty over the effects demonstrated.

Preliminary

Low or very low quality evidence with considerable uncertainty over the effects demonstrated.

Figure 2. Evidence levels

Physical activity pre-treatment

Exercising to increase fitness before undergoing surgery or other therapies (prehabilitation) is encouraged to help patients tolerate difficult treatments and experience fewer complications.¹⁰ Evidence on this subject is emerging, and suggests that exercise training is feasible in the weeks prior to surgery and during neo-adjuvant treatment¹¹ and leads to improvements in physical function. There is also preliminary evidence of fewer post-operative complications and shorter hospital stays, although results have been inconsistent (Table 1). No evidence relating to treatment success or prognosis is yet available.

Table 1. Evidence for physical activity performed before cancer treatment

Outcome	Evidence summa	ry	Evidence level
Physical function	Lung cancer	Cardiorespiratory fitness and lung function were improved in a meta- analysis of 5 RCTs of lower and upper body aerobic training performed pre-surgery. ¹²	Preliminary
	Abdominal cancers (colorectal, liver, bladder)	Small cardiorespiratory fitness improvements were reported from a systematic review of 7 RCTs of walking or cycling programmes in patients undergoing abdominal surgery. ¹³	Preliminary
Post-operative complications	Lung cancer	Fewer post-operative complications and shorter hospital stays were reported from a meta-analysis of 5 RCTs of aerobic exercise programmes. ¹²	Preliminary
	Prostate cancer	Reduced rates of urinary incontinence 3 months after prostatectomy were reported from pre-surgical pelvic floor exercises in a meta-analysis of 6 RCTs. ¹⁴	Preliminary

Physical activity during treatment

During a course of treatment (e.g. chemotherapy or radiotherapy) patients often become physically deconditioned, losing both cardiovascular and muscular fitness, and experiencing fatigue. Traditional advice for combating fatigue centring on energy conservation is counterproductive, since excessive rest worsens treatment-related loss of physical function. This can lead to a vicious cycle of accumulating fatigue and deteriorating function (Figure 3). A promising body of evidence indicates that an appropriate balance of physical activity alongside rest during treatment periods helps to control fatigue and maintain physical function (Table 2).



Figure 3. Vicious cycle of deconditioning, fatigue, and rest

Outcome	Evidence summa	ry	Evidence level
Physical function	All cancers	Exercise programmes undertaken during chemotherapy helped prevent declines in cardiorespiratory and muscular fitness , and even led to small improvements in a systematic review of 14 RCTs. ¹⁵ Similarly, increases in muscular strength were reported from a systematic review of 16 RCTs of patients performing aerobic and/or resistance exercise during chemotherapy or radiotherapy. ¹⁶	Preliminary
	Breast cancer	Moderate improvements in cardiorespiratory fitness (15 RCTs) and small increases in muscular strength (9 RCTs) were reported from meta-analyses of aerobic or resistance exercise. ¹⁷	Promising
	Prostate cancer	Increases in muscular fitness and small improvements or maintenance of cardiorespiratory fitness were observed in men receiving androgen deprivation therapy in a systematic review of 5 RCTs of aerobic and resistance exercise. ¹⁸ Similar results were observed from 4 RCTs of exercise during radiotherapy. ¹⁹	Preliminary
	Haematological cancer	Improvements in cardiorespiratory and muscular fitness were reported in a systematic review of 10 RCTs of exercise interventions performed while hospitalised for stem cell transplantation. ²⁰	Preliminary

Table 2. Evidence for physical activity during cancer treatment

Outcome	Evidence summa	ry	Evidence level
Fatigue	All cancers	Small reductions in fatigue were reported from a meta-analysis of 25 RCTs involving exercise programmes during chemotherapy or radiotherapy. ²¹	Promising
	Breast cancer	Small reductions in fatigue were reported from a meta-analysis of 19 RCTs of aerobic or resistance exercise. ¹⁷	Promising
	Prostate	Fatigue associated with androgen deprivation therapy was controlled or reduced in a systematic review of 5 RCTs of aerobic or resistance exercise. ¹⁸ Reduced fatigue was also reported from a systematic review of 4 RCTs of exercise during radiotherapy. ¹⁹	Preliminary
	Haematological cancers	Reduced fatigue was reported from a systematic review including 3 RCTs of exercise programmes started during hospitalisation for stem cell transplantation. ²⁰	Preliminary
	Head and neck cancers	Control of fatigue symptoms was reported from a systematic review including 2 RCTs exercise performed during radiotherapy or chemoradiation. ²²	Preliminary
Treatment side-effects	Breast cancer	Effects on neuropathic pain were unclear (2 RCTs), while small improvements in shoulder mobility (1 RCT), and a lower risk of lymphoedema (2 RCTs) were reported from a systematic review. ¹⁷ Progressive resistance training, but not aerobic exercise, led to reversal of sarcopenia in a single large RCT. ²³	Preliminary

Outcome	Evidence summa	ry	Evidence level
Wellbeing	All cancers	Slight improvements in depression were reported from a meta-analysis of 6 RCTs, ²⁴ and no clear change in anxiety from 2 RCTs. ²⁵ Improved sleep quality was reported from a meta-analysis of 9 RCTs involving walking interventions. ²⁶	Preliminary
	Breast cancer	No clear effects on depression (5 RCTs), anxiety (2 RCTs), or quality of life (12 RCTs) were demonstrated from a systematic review of exercise during adjuvant therapy. ¹⁷	Preliminary
	Prostate cancer	No clear effects on quality of life were reported from a systematic review of 5 RCTs of aerobic or resistance exercise performed during androgen deprivation therapy. ¹⁸	Preliminary
	Haematological cancers	No clear changes in psychological wellbeing or distress were reported from a systematic review of 4 RCTs of exercise for patients undergoing stem cell transplantation. ²⁰	Preliminary
	Head and neck cancers	Control or improvement of quality of life was reported in a systematic review including 2 RCTs of exercise interventions during radiotherapy or chemoradiation. ²²	Preliminary

Physical activity post-treatment

For patients who have completed treatment, exercise is an important tool in helping restore physical function and wellbeing. Systematic reviews have demonstrated small significant improvements in a range of outcomes following short-term exercise programmes (Table 3).

Table 3. Evidence for physical activity performed after cancer treatment

Outcome	Evidence summa	ry	Evidence level
Physical function	All cancers	Improved outcomes after aerobic and resistance training were observed for both cardiorespiratory fitness (7 RCTs) and muscular fitness (3 RCTs) in meta-analyses. ²⁷	Promising
	Breast cancer	Increases in upper and lower body muscular strength were observed from a meta-analysis of 3 RCTs of resistance exercise. ²⁷	Preliminary
	Lung cancer	Small increases in cardiorespiratory fitness were observed from a systematic review including 3 RCTs of aerobic training for 3 months after lung resection. ²⁸	Promising
	Colorectal cancer	Moderate sized improvements in cardiorespiratory fitness were observed in a meta-analysis of 3 RCTs of aerobic exercise interventions. ²⁹	Promising

Outcome	Evidence summo	iry	Evidence level
Fatigue	All cancers	Moderately sized reductions in fatigue were reported from a meta-analysis of 15 RCTs. ²¹	Promising
	Breast cancer	Moderately sized reductions in fatigue were reported from a meta-analysis of 2 RCTs. ²⁷	Preliminary
	Colorectal cancer	No change in fatigue was reported from a meta-analysis of 3 RCTs involving aerobic exercise. ²⁹	Preliminary
Body composition	All cancers	Small reductions in body weight were observed from a meta-analysis of16 RCTs of aerobic and resistance exercise. ²⁷	Preliminary
	Breast cancer	Slight reductions in body fat percentage were observed from a meta-analysis of 10 RCTs. ²⁷	Preliminary
Treatment side-effects	Breast cancer	Reduction in joint pain was demonstrated in patients taking aromatase inhibitors after a 12-month combined aerobic and resistance training programme in a single RCT. ³⁰	Preliminary
	Prostate cancer	Overall improvements in urinary incontinence were reported from a systematic review of 4 RCTs of pelvic floor training. ¹⁹	Preliminary
Wellbeing	All cancers	Improved outcomes were reported in meta-analyses of quality of life (11 RCTs), and anxiety (4 RCTs) after completing exercise interventions. ³¹ Slight reductions in depression were also demonstrated in a meta-analysis of 9 RCTs. ²⁴	Preliminary

Outcome	Evidence summary		Evidence level
Wellbeing	Breast cancer	Slight reductions in depression (3 RCTs) and small increases in quality of life (6 RCTs) were demonstrated in meta-analyses. ²⁷	Preliminary
	Lung cancer	No change in quality of life was reported from a meta-analysis of 3 RCTs of exercise performed after lung resection. ²⁸	Preliminary
	Colorectal cancer	No change in quality of life was reported from a meta-analysis of 3 RCTs involving aerobic exercise. ²⁹	Preliminary

Physical activity in palliative care

Early systematic reviews of exercise interventions with patients under palliative care all concluded that exercise is feasible and has potential to benefit physical functioning, several symptoms, and quality of life, but RCT evidence was limited.^{32–34} More recent trials provide further encouraging evidence of benefits achievable for patients with progressive disease (Table 4).

Outcome	Evidence summa	ry	Evidence level
Physical function	All cancers	Increases in cardiorespiratory fitness (5 RCTs) and muscular strength (5 RCTs) were reported from a systematic review of exercise interventions for patients with advanced cancer. ³⁵	Preliminary
	Lung	Increases in cardiorespiratory fitness and muscle strength were observed in a trial of 114 patients with advanced inoperable lung cancer after a 6-week exercise intervention during chemotherapy, ³⁶ but no RCT evidence is yet available.	Preliminary
	Prostate	Increases in cardiorespiratory fitness were recorded after a 12-week exercise intervention and maintained 6 months later in a single RCT with men with advanced prostate cancer. ³⁷	Preliminary
	Breast	No clear change in cardiorespiratory fitness was observed from a 16-week home-based exercise intervention in a single RCT of women with metastatic breast cancer. ³⁸	Preliminary

Table 4. Evidence for physical activity performed during palliative care

Outcome	Evidence summa	ry	Evidence level
Fatigue	All cancers	Fatigue was controlled (6 RCTs) or reduced (3 RCTs) in a systematic review of exercise interventions in advanced cancer. ³⁵	Preliminary
	Gastrointestinal cancers	Reductions in fatigue were reported in a single small RCT of an aerobic and resistance exercise intervention during palliative chemotherapy. ³⁹	Preliminary
	Prostate cancer	Clinically relevant improvements in fatigue were reported after a 12-week supervised exercise intervention and maintained over the following 6 months in a single RCT. ³⁷	Preliminary
Body Composition	All cancers	Improvements in bone density in patients with spinal bone metastases were observed 3 and 6 months after resistance exercise training during radiotherapy in a single RCT. ⁴⁰ Furthermore, there was no increase in pathological fracture rate due to exercising.	Preliminary
Wellbeing	All cancers	Improvements in sleep were reported from 2 RCTs and unclear effects on quality of life with 3 RCTs indicating improvements and 6 RCTs reporting no changes in a systematic review of exercise intervention trials. ³⁵	Preliminary

Physical activity and survivorship

Evidence from epidemiological studies is accumulating to indicate that being physically active after a cancer diagnosis is associated with increased survival time and reduced risk of disease progression (Table 5). Given the small number of studies and the observational nature of the research that makes it difficult to control for confounding factors, the evidence is encouraging, but preliminary at this stage. In addition to cancer-specific outcomes, the importance of regular physical activity for helping to prevent or manage other health conditions must be considered. These include cardiorespiratory (e.g. heart disease, stroke, lung disease), metabolic (e.g. obesity, type II diabetes), musculoskeletal (e.g. osteoarthritis, osteoporosis), and psychiatric (e.g. depression, dementia) disorders.⁴¹

Outcome	Evidence summary		Evidence level
Survival and recurrence	Breast cancer	Lower rates of all-cause mortality (8 cohort studies), breast cancer mortality (7 cohort studies) and recurrence or disease progression (3 cohort studies) were associated with higher levels of recreational physical activity in meta-analyses. ⁴²	Preliminary
	Prostate cancer	A lower rate of all-cause mortality and prostate cancer mortality were associated with regular physical activity in a single cohort study, ⁴³ while a reduced risk of disease progression was related to a walking at a brisk pace, regardless of distance walked in another study. ⁴⁴	Preliminary

Table 5. Evidence for physical activity and disease-related outcomes

Outcome	Evidence summa	Evidence summary	
Survival and recurrence	Colorectal cancer	Lower rates of all-cause mortality and colorectal cancer mortality were associated with higher levels of physical activity in studies of women ⁴⁵ and men. ^{46,47}	Preliminary
	Lung cancer	Slightly longer survival (26 months) was observed for patients reporting higher physical activity levels than those who were less active (13 months) in a single observational study. ⁴⁸	Preliminary
	Brain cancer	Slightly longer survival (22 months) was observed for patients reporting higher physical activity levels than those who were less active (13 months) in a single observational study. ⁴⁹	Preliminary

Physical activity guidelines

A review of evidence-based physical activity guidelines for cancer populations from Australia, Europe, and the United States concluded that physical activity should be an integral and continuous part of care for all individuals.⁵⁰ General recommendations common to all published guidelines included:

- Avoid inactivity and return to usual activities as soon as possible after surgery.
- Aim to continue physical activity as far as possible while undergoing treatments.
- Build up to age-appropriate guidelines for health-enhancing physical activity (typically aerobic exercise for two and a half hours per week, resistance exercise twice weekly, and balance/coordination exercise twice weekly)⁴¹ after treatment, heeding key safety principles (Table 6).



Figure 4. Older adult physical activity guidelines

Start Active, Stay Active: a report on physical activity for health from the four home countries' Chief Medical Officers. 2011. Department of Health.

Table 6. Physical activity precautions and contraindications

Potential adverse effect	Safety principles
Exacerbation of symptoms (e.g. pain, fatigue, nausea, dyspnoea)	 Monitor symptoms and modify activity type based on site of treatment (e.g. avoid exercise bike after prostate/rectal surgery Avoid high-intensity activities during symptomatic episodes
Anaemia	 Delay moderate to vigorous intensity activities until resolved
Infection	 Avoid high intensity/volume of activities if immunosuppressed Minimise use of public exercise venues if immunosuppressed, using catheters, or during wound recovery
Falls	 Avoid activities needing considerable balance/coordination (e.g. treadmill, bicycle), if patient has dizziness, frailty, peripheral sensory neuropathy Incorporate muscle strength, balance and co-ordination exercises
Bone fracture	 Avoid high impact or contact activities if patient has bone metastases, or is at osteoporosis risk
Hernia	 Anyone with a stoma should start with low resistance exercise and progress slowly to avoid herniation
Lymphoedema	 To prevent lymphoedema, progress resistance exercises in small and gradual increments To avoid exacerbation of lymphoedema, avoid strenuous repetitive exercise with affected limb, and wear compression garment

Conclusions

There is favourable evidence to support the promotion of physical activity to patients throughout the cancer care pathway. Although some cancer populations have been studied more than others, many of the benefits associated with exercise are relevant for patients with any diagnosis. Therefore the lack of evidence available for some cancers or some outcomes (e.g. cachexia⁵¹, cardiotoxicity⁵²), does not imply a lack of potential value.

The majority of evidence is classed as promising or preliminary due to a combination of factors (e.g. small-sized studies; inconsistent methods or results) that weaken the certainty of the effects demonstrated in systematic reviews. Nonetheless, there is international consensus that exercising before, during, and after cancer treatment is generally feasible, safe, and beneficial for most patients, taking into account the safety principles outlined. Key benefits of exercise prior to treatment include increased physical function which may translate into fewer post-operative complications and shorter hospital stays. Similarly, exercising while undergoing cancer treatment can help prevent decline in physical function and control cancer-related fatigue. After treatment, exercise can contribute to increased cardiorespiratory and muscular fitness, reductions in fatigue, and improved body composition and wellbeing outcomes. In addition, there is potential value of regular physical activity in increasing survival time.

Since physical activity is an important behaviour for multiple outcomes, it is vital that it is maintained on a regular and long-term basis. Many individuals benefit from support to sustain physical activity, and Macmillan provides a range of resources aimed at patients, carers, and healthcare professionals.

Useful resources

There are various drivers of physical activity behaviour in people living with and beyond cancer. If an individual is motivated, confident, focusing on positive achievements and regaining control, with a social network in place, then they are likely to find ways to become active and overcome any physical symptoms and limitations in their physical environment. Conversely, if they are not motivated, confident and suffering from anxiety or depression with no social network, even with few physical symptoms, with plenty of opportunities within their physical environment, they are unlikely to become active⁵³ Healthcare professionals have the potential to cut through these barriers and strongly influence physical activity behaviour.

Health care professionals are uniquely placed to offer physical activity advice to cancer patients during their many interactions throughout the cancer journey at a time when a cancer patient may be motivated to make a lifestyle change.

Macmillan Cancer Support physical activity resources. This includes accredited cancer and physical activity training. https://www.macmillan.org.uk/wonderdrug

Start Active, Stay Active: a report on physical activity for health from the four home countries' Chief Medical Officers. 2011. Department of Health. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/ PublicationsPolicyAndGuidance/DH_128209

American College of Sports Medicine round table consensus statement on exercise guidelines for cancer survivors. 2010. ACSM. <u>http://www.acsm.org/public-information/roundtables</u>

Glossary

Aerobic exercise

Activities performed continuously that promote the circulation of oxygen through the blood and associated with an increased breathing rate and leading to increases in **cardiorespiratory fitness**. Examples of aerobic exercise include brisk walking, jogging, cycling, rowing, stair climbing.

Cardiorespiratory fitness

The ability of the heart and lungs to supply oxygen to skeletal muscles during sustained physical activity. Also known as cardiovascular fitness, aerobic capacity, or exercise tolerance. Cardiorespiratory fitness is achieved through regular **aerobic exercise**, and increased levels are associated with reduced risk of several chronic diseases and overall mortality.

Cohort study

An observational longitudinal study that monitors the same sample of participants (a cohort) over time to examine changes in outcomes and identify possible causal factors. Cohort studies are common in epidemiological research.

Exercise

A form of **physical activity** that represents planned, repetitive movements performed with a specific purpose such as maintaining or improving physical fitness or health. Some activities represent **aerobic exercise** (e.g. brisk walking), others represent **resistance exercise** (e.g. press ups), and some are a combination (e.g. stair climbing).

Meta-analysis

Statistical pooling of results from multiple studies that address the same aim to find the overall effect. Usually included as part of a **systematic review**.

Muscular fitness

The ability of skeletal muscles to lift or move heavy objects (muscular strength) or to continue working without becoming fatigued (muscular endurance). Muscular fitness is achieved through **resistance exercise** and is important for performing activities of daily living.

Physical activity

Any volitional movement of skeletal muscle that results in energy expenditure. Physical activity is therefore a broad term that encompasses general activities of daily living and active transport, as well as planned participation in **exercise** or sport.

Randomised controlled trial (RCT)

An experimental study that randomly allocates participants to receive an intervention (e.g. exercise programme) or a control condition, and compares the outcomes to assess the effectiveness of the intervention.

Resistance exercise

Activities that cause skeletal muscles to contract against an external force, leading to increases in **muscular fitness**. Examples include lifting and lowering weighted objects, or pushing against stretchy bands or one's own body weight as in press ups or leg squats.

Systematic review

A review that follows a predefined protocol to systematically identify and appraise studies on a subject in order to provide unbiased conclusions based on the totality of evidence. Often includes a **meta-analysis** of the data.

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