KNGF Guideline on Oncology

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Koninklijk Nederlands Genootschap voor Fysiotherapie

Royal Dutch Society for Physical Therapy

Vereniging van Oefentherapeuten

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All sections of the guideline, including the summary, are available at **kngf.nl/kennisplatform**.

Koninklijk Nederlands Genootschap voor Fysiotherapie

De fysiotherapeuten van Nederland

VvOCM

Vereniging van Oefentherapeuten

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Table of contents

A General information

A.1 Introduction NOTE

Improvements in (early) diagnosis and new cancer treatments are resulting in an increased number of patients surviving years after their diagnosis. The improved survival percentages are leading to a growing group of people living with the physical and psychosocial consequences of cancer and its treatment. Due to this, cancer is increasingly becoming a chronic disorder by nature.
In addition, there is more and more scientific literature available that describes the positive effects of exercise interventions and physical activity on various health-related outcomes in people with cancer. The new insights have resulted in (inter)national guidelines that recommend physical activity, both during and after the cancer treatment. However, cancer and its treatment can lead to barriers to exercise, therefore possibly necessitating guidance by a physical therapist or exercise therapist. During this guidance the therapist may experience barriers stemming from the complexity of a course of treatment for people living with or after cancer. In many cases, these barriers are generic in nature and are applicable to more than just one type of cancer.
This guideline therefore contains recommendations concerning the physical therapy and exercise therapy treatment of people living with or after cancer. When offering exercise intervention for a specific target group, the therapist has to delve further into the tumour-specific guidelines, which are available in the guideline database of the Federation of Medical Specialists, among others.

Goal of the guideline

This guideline describes recommendations concerning patients experiencing side effects and symptoms of cancer treatment and in whom these side effects make treatment by a therapist more difficult.
The recommendations specifically concern the application of exercise interventions and the associated necessary adjustments in the case of bone metastasis, cardiotoxicity, chemotherapy-induced peripheral neuropathy (CIPN) and fatigue. These aspects are designated as 'complicating factors' in this guideline.
In the general sense, the goal of exercise care is encouraging health and removing barriers to exercise or facilitating exercise and developing and/or retaining as active a lifestyle as possible. Exercise care is aimed at optimising the level of physical capacity, functioning and physical activity and the quality of life in daily life.

Target group

Patient group

This guideline is intended for the treatment of adults who are living with or after cancer for whom physical therapy or exercise therapy treatment may be indicated. The term 'patient' is used in this document for 'the patient of the physical therapist or exercise therapist who has or has had cancer'.

Intended users of the guideline

This guideline is primarily aimed at physical therapists and exercise therapists who treat and guide the patient group defined above. These professional groups are described in the 'Physical Therapist Professional Profile' and the 'Exercise Therapist Professional Profile'. The guideline is also relevant for other healthcare providers who are involved in treating and guiding people living with or after cancer.

Definition

This guideline is aimed at the diagnostic and therapeutic process of the physical therapist and exercise therapist for patients during or after treatment with curative intent or during palliative treatment of cancer. These recommendations apply regardless of the type of cancer a patient has or has had.

Reading guide

The information in the guideline is divided into Section A 'General information', Section B 'Exercise interventions for cancer' and Section C 'Complicating factors'. Section A contains a general introduction, provides background information about the cancer treatment at the time of writing of this guideline and examines the organisation of healthcare with respect to this patient group. Section B contains a general description of how exercise interventions are shaped by a physical therapist or exercise therapist for patients with cancer. Section C contains recommendations for applying exercise interventions for cancer patients if there are factors that may hinder the offering of a therapeutic intervention.
The various topics within a section make up separate, stand-alone modules. In each module, the information is subsequently divided into three levels, with each level going more in-depth into the respective topic:

- The practical tips, the recommendations, are included in the Practice Guideline (the first level).
- Background information and the consideration of the most important arguments that lead to the recommendation are contained in the notes (the second level).
- The Justification (the third level) provides details about how this information was collected (including the search strategy, summary of results, evaluation of the evidentiary value and description of considerations), the process with which this consideration came about and the references of the (scientific) literature used.

Where this document refers to 'he', this can also mean 'she'. Where this document refers to 'therapist', this can mean either 'physical therapist' or 'exercise therapist'. Where this document refers to 'therapy', this can mean either 'physical therapy' or 'exercise therapy'.

Methodology

This guideline was developed according to the KNGF guideline methodology 2019. In addition to this, a KNGF guideline methodology addendum was compiled when developing this guideline, with specific attention being paid to the generic character of this guideline. The way this methodology (including the addendum) was applied and the manner in which relevant external stakeholders were involved in the development are described in the justification of this module.

A.2 Cancer characteristics and treatment NOTE

Cancer is not, in fact, one medical condition but rather an umbrella term that encompasses numerous clinical presentations. There is great variety in biological behaviour and prognosis among the various types of cancer. The common characteristic of cancer is unregulated cell growth, whereby damage to healthy tissue can occur as a result of the space-occupying process (benign tumour) or due to invasive growth of the cancer (malignant tumour). With most types of cancer, spreading of malignant cells occurs through metastasis.
Medical treatment for cancer varies widely, both between various types as well as between the stages of one type of cancer. The goal of a treatment with curative intent is healing. If healing is no longer possible, then palliative treatment is administered which is aimed at inhibiting the disease (or increasing life expectancy) and/or preventing or alleviating complaints and symptoms. Depending on the type of cancer and how far the disease has progressed, one or more treatment types are administered. Treatment options for cancer are surgery, radiation therapy, chemotherapy, antihormonal therapy and targeted therapy. Each of these treatment modalities has its own possible side effects in the form of symptoms, impairments and health risks. These side effects can be both a reason for a need for assistance as well as complicating factors for guidance by the physical therapist and/or exercise therapist.

A.3 Effects of treatment on movement-related functioning NOTE

In many cases, medical treatment for cancer is associated with a loss of function of the musculoskeletal system and related systems. Many patients experience reduced endurance (decreased VO_2max), lower muscle mass and loss of function.
The loss of function of the musculoskeletal system and related systems is multifactorial and a result of both disease processes and the effects of the medical treatment, as well as decreased physical activity during the treatment.
A decreased activity level at the end of treatment helps maintain the reduced physical capacity. The disease or cancer treatment can also affect functioning in daily life and participation, for example due to (chronic) fatigue, limited lung function or pain.

A.4 The role of exercise in cancer NOTE

People living with or after cancer may experience barriers to exercise. These barriers can be practical, social, mental/emotional, behavioural or physical in nature. Additionally, some of these barriers will be a direct or indirect consequence of the cancer or cancer treatment. This is why many people living with or after cancer need guidance with movement-related functioning at some point. To determine which guidance is best for the individual patient, it is important for exercise care to be viewed from a perspective that transcends physical therapy or exercise therapy. The barriers experienced by a patient can be multidimensional in nature, and it is important for this to be noticed in a timely manner. The same applies to recognizing and applying factors that promote movement-related functioning.
When there are barriers to movement-related functioning that can be eliminated with a physical therapy or exercise therapy intervention (for example, [imminent] functional impairment,

[expected] risks related to the clinical state or mental/emotional barriers that require a specific therapeutic approach), patients will need guidance from a physical therapist or exercise therapist. This guidance can consist of counselling (e.g. through motivating talks), advice about safely and effectively performing certain actions or exercises and advice about choices for independent exercising with a specific intended effect, but can also consist of fully or partially supervised exercise intervention.

A.5 Organisation of healthcare NOTE

Physical therapy and exercise therapy are pre-eminently the professional groups that deal with exercise care. Registered oncology physical therapists and general physical therapists and exercise therapists specialised in oncology rehabilitation sciences have become skilled in guiding patients confronted with a cancer diagnosis; an exploration and specialisation that was set in motion in the 1990s.
Due to the complexity of a course of treatment, a specialised oncology physical therapist or other specialised physical therapist may be necessary during an intake or when carrying out the treatment plan. It is therefore important for a therapist to be conscious of his own skills and refer the patient in a timely manner, when necessary. The general principle of 'unskilled is unauthorised' applies here.

It is important for existing deviations or contraindications to be known to the treating therapist before the physical therapy or exercise therapy intervention is started. This necessitates a proper transfer from the physician or general practitioner, which includes the relevant information about complaints, symptoms and the treatment. Good supervision during the intervention and mutual communication between the participating healthcare providers when conducting an exercise intervention are essential.

The therapist will also have to consider for each individual patient whether the patient needs additional guidance, e.g. occupational therapy, dietetics, podiatric therapy or cognitive behavioural therapy. Due to possible reimbursement from basic healthcare insurance, a referral from the physician or general practitioner is needed in some cases for disciplines outside of physical therapy or exercise therapy.
When offering exercise intervention for people who are living with or after cancer, it is important to consult within the network of professionals, but also with the treating medical specialist and, if appropriate, the Company Physician Oncology Consultant ('BACO').

B Exercise interventions for cancer

B.1 Choice of exercise intervention NOTE

The content of the exercise intervention is determined by the treatment phase, the patient's individual goals and wishes, the capacity level (both physical as well as mental/emotional), the degree of trainability, the behaviour and the patient's preferences for training tools.
Independently continuing exercising after the therapist's guidance ends must be a point of attention from the start of the guidance and requires customised advice. In this context, exercise can be both intentional exercise (exercise as a goal) as well as functional exercise (exercise as a means to achieve other life goals).
Regardless of the phase in which the patient is, the guidance can consist of the following components:

- encouraging exercise and providing advice about this;
- optimising activities that are relevant for the patient, and optimising the functions and anatomical characteristics that constitute a prerequisite for exercise, and teaching the patient to maintain these;
- combating complaints and barriers that the patient experiences during exercise;
- promoting behavioural change towards an active lifestyle.

B.2 Training recommendations NOTE

The general recommendations for physical activity for promoting general health in people living with and after cancer largely follow the recommendations for physical activity in adults with a chronic condition.
Here the aim is performing aerobic activity three times per week for at least 30 minutes each time and strength training on two or more days per week for 20 minutes each time.
Daily stretching exercises should preferably be added to this activity, as well as possibly specific exercises based on the health status and the disease's side effects related to the treatment (e.g. coordination and balance exercises). The minimum exercise advice for people living with or after cancer is to avoid inactivity and be as active as possible. Training recommendations for a number of specific outcomes are included in the explanation for this module.
The exercise programme should be optimised so that it is aligned with the need for assistance. This may mean a deviation from the general recommendations.

Some patients may not initially be able to stick with the recommended exercise recommendations. The therapist therefore plays an important role when it comes to advising, supporting and motivating the patient to work as much as possible towards the desired training parameters and the desired load level.

The recommendation is to base the training intensity on physiological parameters (heart rate, clinical symptoms of exertion) and the perceived exertion level.

B.3 Measurement instruments NOTE

In order to choose from among the many available tests, the relative importance of the test must be weighed against the clinimetric properties, safety and practicality (including the patient's load) of the test. The explanation includes measurement instruments that are often used in oncology problems.

B.4 Personalised guidance NOTE

The goal of the treatment is to take patients to such a level of functioning in the short and medium to long term that autonomous healthy exercise behaviour is possible. Here the therapist looks for the correct form of exercise in relation to the physical possibilities that someone (still) has. In consultation with the patient, the therapist can devise a customised exercise intervention. The therapist can help eliminate or decrease impediments the patient is experiencing as a result of the illness or cancer treatment and which are the reason for not achieving the desired activity level.

B.5 The safety of exercise interventions NOTE

Attention to complaints due to side effects and (possible) long-term effects of the treatment is important with an aim to set (achievable) goals, protect safety in the training situation and prevent and detect overburden in a timely manner.
Based on the patient's complaints or impairments and the medical treatments they've undergone, it must be considered in each individual case whether exercise makes sense and whether the patient can be trained.

C Complicating factors

C.1 Bone metastasis NOTE

Recommendations

Consult with the referrer to see if there is stable bone metastasis. Supplementally, collect as much information as possible that is important to the physical therapy or exercise therapy treatment; especially in connection with the risk of occurrence of a (pathological) fracture or compression of the spinal cord. This information must entail at least the following:

- the location and type of bone metastasis (as detailed as possible);
- the presence of neurological symptoms;
- the presence of osteoporosis;
- the presence of pain related to the location of the metastasis;
- prior fractures;
- the treatment administered due to the bone metastasis;
- the assessment of the risk of falling.

Reassess this information periodically.

Consult with the treating physician or nursing specialist to come up with a suitable physical therapy or exercise therapy treatment plan.

Prior to starting an exercise intervention, consult with the patient and weigh the benefits and disadvantages. When doing so, include the following:

- the risks of the exercise intervention designated by the physician (such as the risk of fractures or spinal cord compression);
- the degree to which the exercise intervention can be adapted in order to minimise the risks;
- potential benefits of exercise intervention and the health risks of not exercising, such as the risk of falling due to inactivity and the associated increased risk of fractures.

Offer customised exercise intervention and take into account the location and type of bone metastasis. Adjust the way in which exercise is performed based on the location of the bone metastasis, if necessary.

Preferably offer supervised exercise intervention to patients with bone metastasis. For patients who prefer exercising independently, at minimum give them instructions on how to safely and effectively perform the exercises.

Avoid transverse and/or compression forces at a location with proven metastasis in order to decrease the risk of a fracture. This also applies to performing the exertion diagnostics.

Preferably administer exercise intervention with as much functional training as possible. Consider using the patient's own body weight (gravity) during this training instead of equipment and dumbbells. Formulate clear goals together with the patient and communicate expectations.

Do **not** start working with patients with **unstable bone metastasis** without first doing a comprehensive risk assessment in consultation with the treating physician and any other involved practitioners.

Offer patients with **unstable bone metastasis** an exercise programme or exercise instructions with a focus on functional exercises within the boundaries as agreed in a multidisciplinary team.

C.2 Cardiotoxicity NOTE

Recommendations

Consult with the treating physician about requesting a maximal exertion test with ECG and respiratory gas analysis based on risk factors for decreased cardiac capacity and clinical decision-making. See the following table.

Risk factors for decreased cardiac capacity in people living with or after cancer.
Source: Henning, 2017

Medication-related risk factors

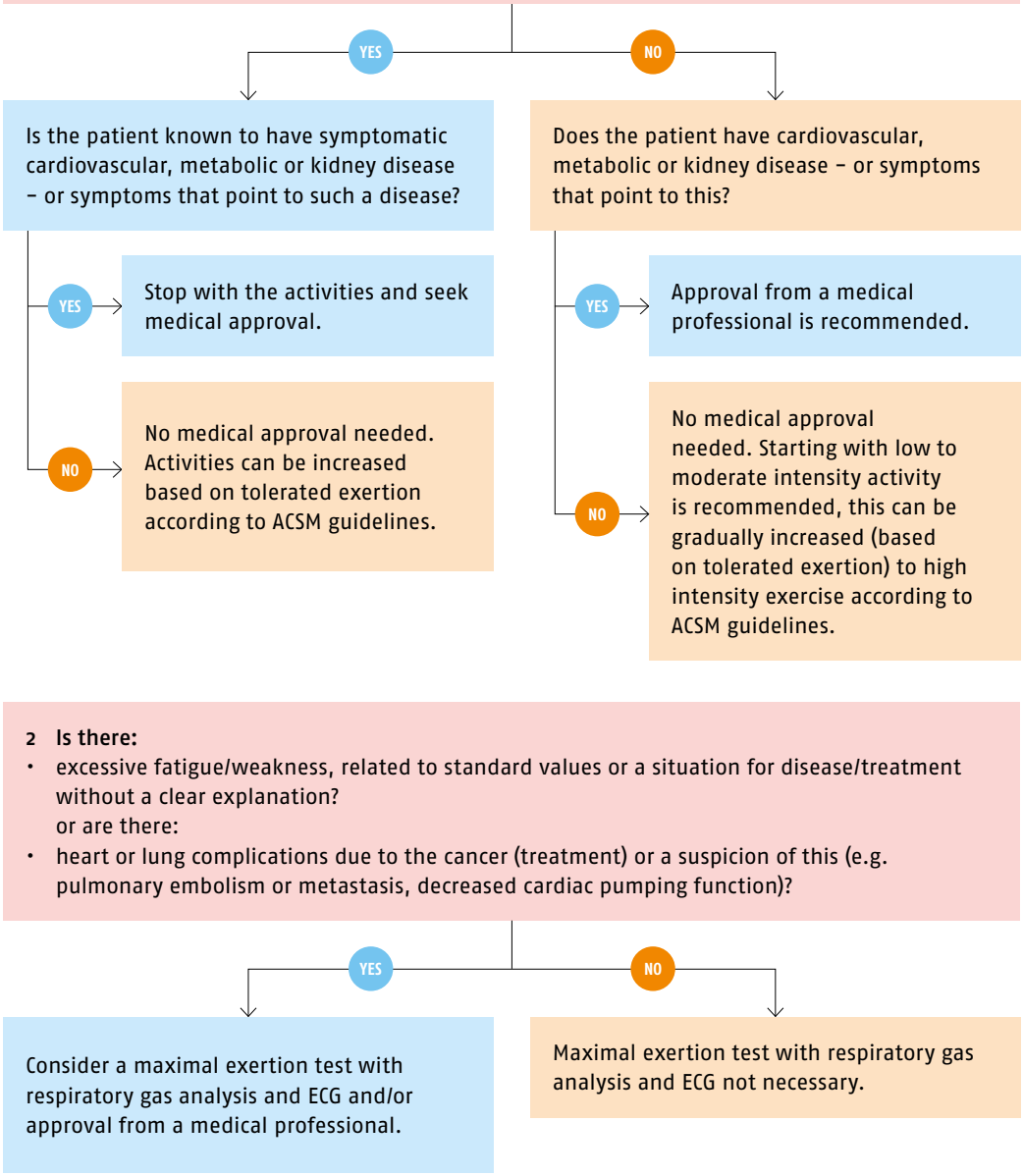
high risk	anthracyclines (doxorubicin, mitoxantrone, epirubicin, daunorubicin and idarubicin), cyclophosphamide, ifosfamide, clofarabine)
moderate risk	trastuzumab, pertuzumab, sunitinib, sorafenib, imatinib
low risk	bevacizumab, dasatinib, imatinib, lapatinib
sporadic risk	etoposide, rituximab, thalidomide

Patient-related risk factors

- cardiomyopathy or heart failure
- coronary disease and/or peripheral vascular disease
- hypertension
- diabetes
- previous or simultaneous treatment with anthracycline
- previous or simultaneous radiation of the thorax
- age >65 years
- being female

The diagram for assisting the clinical decision-making process is depicted in the following figure.

Clinical decision-making process prior to the exercise intervention



ACSM = American College of Sports Medicine; ECG = electrocardiogram.

Use the results of the maximal exertion test to:

- determine whether physical training can be administered;
- identify limiting factors;
- make an informed decision for types of therapy and the intensity of the physical training.

Discuss any risks for cardiovascular incidents with the patient. Prior to commencing the exercise intervention, conduct a risk-benefit analysis together with the patient. Consider the following in this analysis:

- the risks of the exercise intervention (such as risks of cardiovascular incidents);
- the degree to which the exercise intervention can be adapted in order to minimise the risks as much as possible;
- potential benefits of exercise intervention and the health risks of not exercising.

Avoid valsalva manoeuvres (forcefully 'detaining' the breath in order to increase intra-abdominal and intrathoracic pressure) in patients with cardiovascular complaints due to cancer treatment in connection with the associated acute increase in blood pressure.

C.3 Chemotherapy-induced peripheral neuropathy (CIPN) NOTE

Recommendations

For patients at risk of developing CIPN, be alert to signs of neuropathy if these have not been observed in the past. These signs are listed in the box below.

Symptoms of chemotherapy-induced peripheral neuropathy (CIPN) (Source: Scheel, 2014)

- Tingling and prickling sensations
- Strange feeling in the hands and feet
- Disrupted tactile sense
- Decreased pain sensation or shooting pain
- Decreased sensitivity to temperature
- Numbness
- Weakness or reduced muscle strength or function
- Coordination problems

Advise patients with (a change in) neuropathy complaints to discuss these complaints with the medical oncologist or GP.

Consider offering an exercise intervention to patients with CIPN, preferably as soon as possible after the onset of complaints.

Consider making adjustments in the exercise intervention based on the complaints of the individual patient with CIPN, insofar as these adjustments are necessary for being able to safely and effectively implement the desired exercise programme.

Use the Timed Up & Go (TUG) test or the Fullerton Advanced Balance (FAB) scale for assessing the functional mobility and risk of falling of patients with CIPN who indicate that they experience balance problems or in whom you suspect balance problems.

Encourage and motivate the patient with CIPN to exercise the part of the body where the neuropathy is manifesting.

Consider an intervention aimed at behavioural change or pain education (if needed, by a specialised therapist) in patients with CIPN who are limited due to pain or discomfort.

Offer patients with CIPN guidance aimed at decreasing or preventing fear of movement.

C.4 Fatigue NOTE

Recommendations

Offer supervised exercise intervention to patients with cancer-related fatigue.

When taking the medical history, assess factors that impact fatigue (including processing problems, fear of a relapse, dysfunctional cognitions, irregular circadian rhythm, overactivity or underactivity and unrealistic expectations from the patient's environment).

Consider multidisciplinary treatment or a cognitive behavioural approach in the following situations:

- The patient is already experiencing severe fatigue at the moment of the cancer diagnosis.
- The patient experiences anxiety/tension, depression or sleep problems.
- There is no progress after a 12-week exercise intervention, despite adequate physiological stimulus.

If this appears to be indicated based on the mentioned situations, consult with the treating physician about a referral for cognitive behavioural therapy and about continuing the exercise intervention.

Use the Multidimensional Fatigue Inventory (MVI-20) to assess cancer-related fatigue and evaluate when there is a reason for this based on the medical history.

Determine the duration of an exercise intervention based on the starting level and set goals, but consider offering exercise intervention for at least 12 weeks with a frequency of three days per week, with at least moderately intensive training.

Offer customised exercise intervention. When doing so, take into account the symptoms and impairments the patient experiences. In addition to the FITT principles (frequency, intensity, type and term) and training progression during the exercise intervention, also pay attention to the overall activity regulation.

Consider High Intensity Interval Training (HIIT) for patients who prefer this and who have sufficient exercise skills. Start with patients who cannot perform HIIT due to inhibiting co-morbidity, too low initial fitness or other symptoms and impairments, with an exercise intervention of continuous intensity.

Explanation

Note A.1 Introduction

The Practice Guideline explains the reason for and the objective of this guideline. This section of the guideline contains an explanation of the FAST project and a description of the most important terms in this guideline. The KNGF Guideline on Oncology was developed in accordance with the 2019 KNGF Guideline Methodology (KNGF 2019). The justification of this module describes how this methodology was applied to this specific guideline.

FAST project

Developing guidelines is an expensive and long process, and the way in which this process has been defined for physical therapy and exercise therapy (specifically, at the diagnosis/condition level) is not always aligned with daily healthcare practice. Based on the physical therapy and exercise therapy system advice, research was done on the possibilities of developing all-condition-encompassing guidelines for physical therapy and exercise therapy in a more efficient manner (Healthcare Institute of the Netherlands 2016). At the beginning of 2018, the VUmc (since 7 June 2018 Amsterdam UMC, location VUmc) and Ecorys compiled an action plan for the development of such all-condition-encompassing guidelines (both generic and domain-specific), due to which topics with mutual elements no longer need to be elaborated separately for each condition-specific guideline (VUmc/Ecorys 2018). The generic guidelines concern aspects of healthcare that can be applicable to all patients who see a healthcare provider, such as self-management. The domain-specific guidelines concern aspects of healthcare that can be applicable to all patients who have closely related conditions, such as oncological conditions, the topic of this guideline.
This advice from the VUmc and Ecorys was implemented in the FAST (Fysio-/oefentherapie Aanpak Stroomlijning kwaliteitsstandaarden [Physical/Exercise Therapy Approach Streamlining of Quality Standards]) project.

The FAST project is comprised of the following:

- **Sub-project 1** Development of an addendum to the KNGF guideline methodology for the development of generic/domain-specific guidelines and process evaluation.
- **Sub-project 2** A proof-of-concept of a generic guideline with 'self-management' as the topic.
- **Sub-project 3** A proof-of-concept of a domain-specific guideline with 'oncology' as the topic.

If the action plan appears to be feasible and produces relevant guidelines for the professional field, the addendum (sub-project 1) will be incorporated into the KNGF guideline methodology (KNGF 2019). This can then also be used to develop other generic and domain-specific guidelines (also by other paramedical professional groups) in the future.
By referring to these generic and domain-specific guidelines in condition-specific guidelines and not having to answer similar clinical questions multiple times, which is currently the norm, guideline development within physical therapy and exercise therapy will be able to take place more efficiently.

Status of a guideline

Recommendations in a guideline are not laws or mandatory rules. In principle, therapists should adhere to the provisions of the guideline, but substantiated deviation is legitimate and even necessary if this is commensurate with the individual patient's situation and wishes (AQUA 2021).

Most important definitions and terms

- Adjuvant: additional to the primary treatment
- Aerobic: exercise whereby the body produces energy with the help of oxygen
- Antigen: a protein on a cell membrane by which a tumour cell can be recognised
- Anthracyclines: collective name for a group of cytostatics
- Apoptosis: programmed cell death
- Bone marrow suppression: decreased function of the bone marrow, resulting in a lowered blood cell count
- Cachexia: decrease of muscle mass and unintended weight loss
- Cardiomyopathy: heart muscle disease causing less blood to be pumped around
- Cell division: process whereby the cell splits itself up into two or more new cells
- Continuity (surgery): the surgical preparation consists of one part (goal: the tumour is not incised)
- Curative: intended to cure
- Cytostatics: medications that have an inhibiting effect on the splitting of (tumour) cells
- Cell differentiation: process where a (stem) cell develops into a cell with tissue-specific properties
- DNA: molecule that acts as the most important chemical carrier of genetic information
- Dyspnoea: shortness of breath
- ECOG performance status: benchmark for how well a person is able to perform activities of daily life developed by the Eastern Cooperative Oncology Group
- Fibrosis: hardening due to excessive connective tissue formation in an organ or tissue
- Induration: localised hardening of tissue
- Infiltration/invasive growth: slow penetration (e.g. cancer cells that grow into healthy tissue)
- Initiation (cell): mutation in genetic material without the damage being repaired
- Ionising radiation: high-energy radiation leading to the formation of free oxygen radicals
- Malignant: malicious
- Metastasis: spreading of a primary malignant tumour; osteolytic metastasis is characterised by a breakdown of bone, causing the bone to become weak and brittle
- Mucositis: inflammatory reaction of mucosa
- Mutation: change in the DNA
- Neoadjuvant: prior to the primary treatment
- Neuropathy: neurological condition where one or more nerve(s) no longer work(s) properly
- Oedema: accumulation of fluid in a body part
- Oestrogen: female sex hormone
- Osteoporosis: severe bone decalcification
- Ovariectomy: procedure during which one or both ovaries are removed
- Palliative: aimed at disease inhibition and symptom alleviation but not at curing
- Premalignant: abnormality that is not (yet) malignant, but not entirely benign either

- Promotion (cell): stimulation of cell growth through mutation
- Radical resection: complete removal of the tumour with tumour-free cutting edges
- Sarcopenia: loss of both muscle mass and muscle function
- Sentinel lymph node: lymph node that is the first to collect the lymphatic fluid from the area around the tumour
- Testosterone: male sex hormone PRACTICE GUIDELINE

Note A.2 Cancer characteristics and treatment

Surgery

The goal of surgical treatment is to remove the tumour tissue entirely, with the intent to cure the disease. With a surgical procedure, the aim is to achieve 'continuity' (the surgical preparation consists of one part; the tumour is not incised), 'radicality' (the tumour is completely removed) and sufficient margin up to the healthy tissue.
Surgery is often applied in combination with other treatment modalities prior to (neoadjuvant) or at the end (adjuvant) of the surgery. Surgery can also be used in direct combination with other therapies, such as radiation therapy (where the direct surroundings of the tumour in the body are radiated pre-operatively) or chemotherapy (e.g. flushing the abdominal cavity with medications in addition to surgical removal of the tumour in the event of metastasis in the peritoneum).
With surgical removal of the primary tumour there may be an indication for removal of the locoregional lymph nodes. If possible, the sentinel node procedure is applied, a procedure used to identify the lymph node where the tumour area drains first with the help of imaging. This so-called sentinel lymph node is removed and examined by the pathologist. If the cancer cells are missing in the lymph node, then a complete lymph node resection is not performed.
Surgery is not used as a form of curative treatment for haematological tumours and lymphatic system diseases. In the palliative phase, surgery can be used to remedy or decrease complaints.

Radiation therapy

Radiation therapy is the exposure of tissue to targeted, high-energy radiation. External radiation equipment can be used for the irradiation, as can small radiation sources that are administered to the patient (so-called brachytherapy).
A new form of radiation therapy called proton therapy has been in use in the Netherlands since 2018. Here small charged particles from the atomic nucleus (protons) are used instead of photons or electrons. This makes proton therapy especially suited for patients with tumours located close to vulnerable organs and for patients in whom traditional radiation therapy causes many side effects.
The mechanism of action of radiation therapy relies on the ionising effect of X-ray irradiation. Free oxygen radicals are formed in the irradiated tissue due to this ionisation of molecules, which subsequently damage the DNA of the cells. The radiation therapy is dosed and administered so that a maximal effect is achieved on the tumour and minimal damage is caused to healthy tissue. Recovery of healthy tissue is primarily facilitated by dividing the radiation dose into repeated small fractions. That's because healthy cells in the tissue can repair the damage – up to a certain extent – in the intervening periods. Malignant cells are not able to repair the DNA damage and die after irradiation during the cell division.
Radiation therapy can also be applied in combination with chemotherapy, with the chemotherapy enhancing the effect of the radiation therapy. Radiation therapy can be administered both as

adjuvant therapy (as a supplement to the primary treatment) and as neoadjuvant therapy (prior to the primary treatment), either in combination with other treatments or standalone. Radiation therapy can also be used during the palliative phase for alleviating pain, for example.

Chemotherapy

Chemotherapy entails administration of medications called cytostatics. Depending on the situation, the cytostatics are administered by means of infusion, tablets, injections or a catheter. They inhibit cell division (the process whereby the cell splits itself up into two or more new cells) or kill cancer cells. They can reach cancer cells at almost any location because they spread through the blood. In some cases cytostatics are administered in the cerebrospinal fluid.
Cytostatics are mostly used as adjuvant, neoadjuvant or palliative treatment in the form of a cure (chemotherapy). Usually various substances are combined in such a cure, each with its own treatable trait. A comprehensive overview of the substances and their possible side effects can be found on the website of the Dutch Association of Comprehensive Cancer Centres, and on the website of the Pharmacotherapeutical Compass.

Antihormonal therapy

Some tumours depend on sex hormones (the female sex hormone oestrogen and the male sex hormone testosterone) in order to grow. Antihormonal therapy blocks the effect of hormones or inhibits the production of hormones. Deactivating the gonads can influence the hormonal environment. This can be done through surgery (removal of the ovaries or testes), through radiation therapy or with medications.
Antihormonal agents work by inhibiting the production of oestrogens in tissue other than the ovaries or by counteracting the effect of oestrogens (tamoxifen) or testosterone (gonadorelin agonists). They can be used as adjuvant, neoadjuvant or palliative treatment.

Targeted therapy

Targeted therapy is treatment with medications that – different from chemotherapy – are specifically aimed at (processes in) tumour cells. There are two groups of targeted therapy: monoclonal antibodies and small molecules.
Monoclonal antibodies are produced in the laboratory. They detect the antigen (a protein, in this case situated on the cell membrane) of a cancer cell and bind to it. The binding impedes the growth processes or the new formation of blood vessels of the tumour cell or even sets apoptosis (programmed cell death) in motion. There are also monoclonal antibodies that stimulate the immune system, due to which the manner of growth of cancer cells is impeded or cancer cells are killed.
Small molecules are medications that very specifically act on processes and signals that are responsible for the growth, division and survival of cancer cells.
Targeted therapy is often administered in combination with other treatments, both in the (neo) adjuvant as well as the palliative phase. PRACTICE GUIDELINE ^

Note A.3 Effects of treatment on movement-related functioning

Decreased endurance has been described in various studies (Courneya 2007, 2009; Jones 2007, Van Waart 2015). The VO_2max, – the most important marker for endurance – is associated with quality of life (Herrero 2006); functional independence is at risk with low endurance (Shephard 2009). The VO_2max of patients with breast cancer is an average of 25% lower after treatment with

chemotherapy than for healthy inactive women (Peel 2014). Decreases in muscle strength and muscle mass can also occur in people living with or after cancer (Vega 2016). Low muscle mass has been associated with higher treatment toxicity, decreased chance of survival and lower quality of life (Blauwhoff-Buskermolen 2016; Kurk 2019; Vega 2016).
A complete description of all the negative effects of cancer and cancer treatment is outside the scope of this guideline and can be found on the websites of the KWF and the IKNL, among others. A brief overview of the most relevant effects within the framework of exercise interventions is provided below. For more detailed information, please refer to the available textbooks and available tumour-specific guidelines.

Effects of surgery

The effects of surgical treatment on movement-related functioning depend on the location and comprehensiveness of the surgery. Hospitalisation and surgery can lead to decreased physical capacity (Van Rooijen 2019) and can (especially in the elderly) affect mobility and the condition. The scar can cause limited range of motion and there may be motor or sensory nerve damage. Surgical removal of lymph nodes can be a cause of the onset of lymphoedema (Schmitz 2010). Prostate removal often leads to incontinence and, just like the placement of a stoma – on the colon or small intestine, for example – causes limitations for types of training that include high intra-abdominal pressure and for contact sports (Schmitz 2010; Heydenreich 2020). In the case of reconstructions, there may be a temporary restriction regarding exercise or load.

Effects of radiation therapy

The side effects of radiation therapy first manifest themselves in rapidly dividing tissue. Depending on the location of the irradiation, patients may experience complaints such as mucositis (inflammation of mucosa, e.g. in the mouth, lungs or intestines), redness and skin sensitivity. These early responses are often reversible.
Late responses (such as radiation fibrosis) occur months to years after treatment has ended in slower dividing tissue and are often irreversible. Radiation fibrosis manifests as decreased elasticity in combination with induration (hardening) of the tissue. Radiation therapy can cause the onset of lymphoedema due to loss of function of lymph nodes or lymphatic vessels or due to fibrosis of the skin and subcutaneous connective tissue (Barazzuol 2020).
In the very long term, radiation therapy can also cause nerve damage. Depending on the dose, radiation therapy on muscle tissue can cause local dysfunction and an inability to hypertrophy. This applies to both the skeletal muscles and the heart muscle.

Effects of chemotherapy

The side effects of chemotherapy and the consequences thereof on movement-related functioning are very varied and can differ from person to person, even when administering the same substances. Heart damage can occur after treatment with anthracyclines (Kirkham 2019).
This damage can result in heart failure and have a negative impact on exercise tolerance. Bone marrow suppression, a decreased functioning of the bone marrow that leads to a decrease in number of blood cells, occurs with a large number of cytostatics and can lead to a lower number of white blood cells and a (temporary) decrease of the haemoglobin level, which results in an increased risk of infection, fatigue and reduced exercise tolerance (Jones 2009). The level in anticoagulant factors can also decrease, creating a higher risk of bleeding during large loads or concentrated loads. Bone marrow suppression agents (such as G-CSF) can cause bone or muscle

pain, but this pain is not a contraindication to exercise. Neuropathies can lead to sensory disorders and loss of strength. Hand-foot syndrome is a combination of sensory neuropathy, redness, swelling and sometimes blister formation on the hands and feet which is exacerbated by pressure or frictional forces.
During and after chemotherapy treatment, the body composition can change due to a combination of metabolic factors and behavioural change, with decreased muscle mass occurring which can be accompanied by increased fat mass (Pedersen 2017). A changed body composition, in turn, can result in decreased exercise tolerance, especially for activities where muscle strength is important in relation to body weight (e.g. walking and stair-climbing).

Effects of antihormonal treatment

Antihormonal therapy aimed at oestrogen results in premature induction of menopause, thereby creating an increased risk of osteoporosis. Antihormonal therapy can also be accompanied by (non-inflammatory) joint problems, mood changes and feelings of depression. High doses of progestogens can also lead to peripheral oedema and muscle cramps, among other things.
In women, antihormonal treatment can result in hot flushes and increased fat mass and decreased fat-free mass. In men, antihormonal treatment can lead to weakness and weight gain, increased fat mass and decreased fat-free mass (Smith 2002). Men also have an increased risk of cardiovascular disease (Boland 2021), a greatly increased risk of falling due to physical changes such as weakness and a slow walking pace and a low degree of physical activity (see Vulnerability), especially if they are also overweight (Winters-Stone 2017). Here too, there is decreased bone mineral density, which can ultimately lead to osteoporosis (Galvao 2008).

Effects of treatment with targeted therapy

There is generally not a lot known about the effects of targeted therapy on exercise capacity. One exception is the monoclonal antibody trastuzumab, which is often used for specific types of breast cancer. It has a (reversible) cardiotoxic effect. In contrast to anthracyclines, with trastuzumab there is no cell death but rather cell dysfunction. Due to this, a decreased function of the left ventricle can occur (Procter 2010). Therefore, a standard screening for left ventricle functioning is done when administering treatment with trastuzumab. Excessive decrease of this function is a reason to discontinue or stop the treatment. Symptomatic heart failure due to trastuzumab is therefore very rare.
Treatment with trastuzumab is therefore not seen as a contraindication for exercise. It is important for the therapist to be alert to signs of heart failure during exercise (especially dyspnoea (shortness of breath) during exertion, sudden weight gain or peripheral oedema), in particular if the patient was previously treated with anthracyclines (e.g. adriamycin, doxorubicin; see C.2 'Cardiotoxicity').
Other means that are used as targeted therapy can have similar effects on factors related to the exercise capacity. A comprehensive description of the side effects and effects of targeted therapy can be found at www.bijwerkingenbijkanker.nl. PRACTICE GUIDELINE

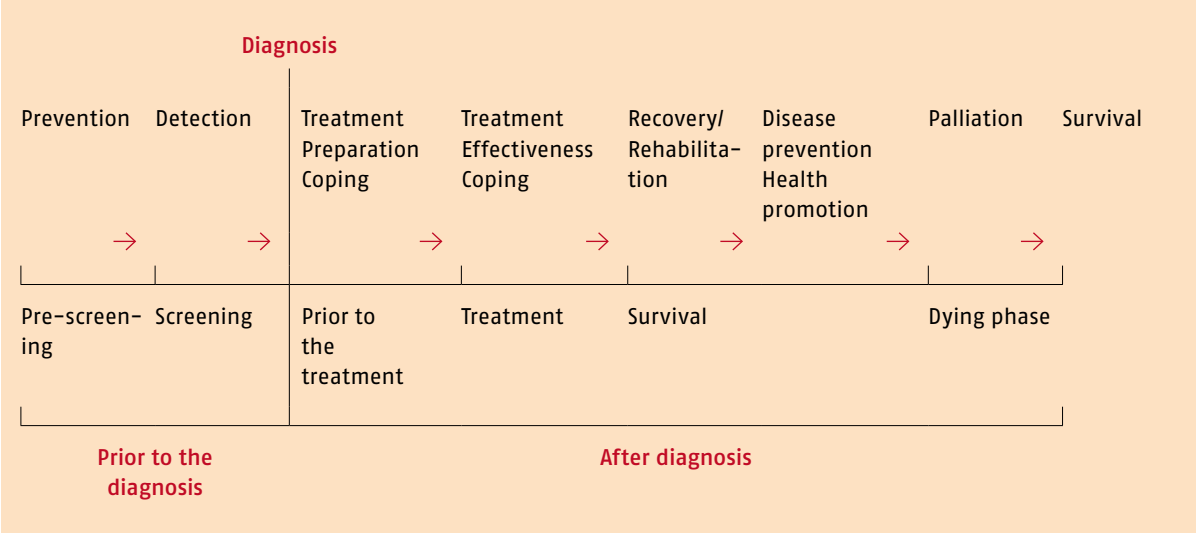
Note A.4 The role of exercise in cancer

The therapist encourages people living with or after cancer to be sufficiently physically active. Although many people adhere to a healthy diet and stop smoking after being diagnosed with cancer, the impact of cancer on exercise behaviour is often negative (Courneya 1997; Schwartz 1998). People living with or after cancer generally exercise less than comparable groups without

chronic conditions (Eng 2018; Ooijendijk 2006). They may experience barriers to exercise. These barriers can be practical, social, mental/emotional, behavioural or physical in nature. Additionally, some of these barriers will be a direct or indirect consequence of the cancer or cancer treatment. This is why many people living with or after cancer need guidance with movement-related functioning at some point.

PACC framework

In order to organise research and exercise care during and after cancer treatment and have it take place in a more targeted manner, researchers outlined a framework for physical activity and cancer, the so-called 'PACC framework' (Courneya 2007); see the following figure.



Dutch translation of the Physical Activity and Cancer Control (PACC) framework (Courneya 2007)

The PACC framework differentiates between prevention, the phases prior to the diagnosis, the phases during treatment and the phases after the treatment has ended. The primary goals of exercise interventions in the various phases are: 1) cancer prevention during the phase prior to a diagnosis, 2) preparation for the treatment in the phase after the diagnosis and prior to the treatment (prehabilitation), 3) increase of the effectiveness of the treatment and limitation of negative effects in the phase during the treatment, 4) functional recovery and disease prevention (both cancer relapse and prevention of other conditions, including cardiovascular conditions), after the curative treatment has ended, and 5) symptom alleviation and retention of patient autonomy in the palliative phase. All of these phases will be examined in more detail later.

Prevention

Primary prevention describes the activities that prevent the onset of disease (Adami 2001). Compliance with guidelines for cancer prevention is associated with a smaller chance of the onset of cancer (Kabat 2015). These guidelines contain recommendations for maintaining a healthy body weight, sufficient physical activity and a healthy diet (Kushi 2012). The association between physical activity and the risk of the onset of cancer has been primarily researched in observational studies.

Based on these studies, strong evidence has been found for a preventive effect of sufficient exercise on the risk of breast, colon, endometrial, bladder, oesophageal, kidney and stomach cancer (Patel 2020). The recommended amount of physical activity for preventing these types of cancer is 150 to 300 minutes per week of aerobic training of at least moderate intensity, or 75 to 150 minutes of intensive aerobic training (ACSM 2019). More research is needed in order to compile targeted recommendations for the optimal amount of physical activity for preventing cancer.

Prehabilitation

Prehabilitation is care prior to an operation with the goal of preparing a patient physically and mentally/emotionally for the surgery, promoting the recovery and decreasing complications. Prehabilitation is usually multimodal with a behavioural change programme (such as stopping smoking), dietary counselling, mental or emotional support and/or physical therapy or exercise therapy. The success of prehabilitation depends on the effort and cooperation of all those involved: both the patient and his/her loved one(s) as well as all (in)directly involved healthcare providers. With a number of types of cancer, such as colon cancer, prehabilitation was found to be feasible, safe and effective, but for other types of cancer evidence for its effectiveness is limited (Bobbio 2008; Van Rooijen 2019). Nevertheless, this type of care is now being implemented in many places. Research has shown that endurance and physical strength can increase, the hospitalisation duration can be shorter and the functional capacity can recover faster with prehabilitation (Van Rooijen 2019). Prehabilitation appears to be most successful in people with a high risk of complications or delayed or insufficient functional recovery (Berkel 2021; Thomas 2019).

During treatment

The therapist advises patients to avoid inactivity and to aim to follow the advice in the guidelines for physical activity for people with cancer: 3x per week aerobic training for 30 minutes and 2x per week strength training for 20 minutes (ACSM 2019). See the advice regarding the FITT principles in B.2 'Training recommendations'.

It is important for the therapist to seek out a training level that is both effective and feasible for the patient. The patient's capacity can fluctuate greatly during the treatment, which requires continuous reconsideration and (where necessary) adjustment of the training programme. Training during cancer treatment focuses on decreasing the side effects of the treatment, combating decreased physical capacity, facilitating continuation of the treatment and possibly improving the effectiveness of the treatment.

Results of systematic review have shown that there is strong evidence that targeted physical activity during treatment can at minimum decrease, if not improve, some of the treatment-related reduction in muscle mass, muscle strength, endurance and fatigue (Lee 2020; Sweegers 2019; Van Rooijen 2018; Van Vulpen 2020). Physical activity during the treatment may also improve certain aspects of quality of life (Buffart 2017; Lipsett 2017; Sweegers 2018). Exercise interventions in this phase are the most effective when they are performed under guidance (Buffart 2017; Campbell 2019; Sweegers 2018). There is reason for guidance (by a physical therapist or exercise therapist) within the framework of healthcare with a treatment with high symptom burden and/or rapidly changing capacity (Campbell 2019; Schmitz 2019). The Enhanced Recovery After Surgery (ERAS) programme can be employed with regard to an operation (including colorectal, thoracic, gynaecological and urological). This is a quality programme which combines various factors that have a positive effect on recovery (NVH 2020). A part of this programme is the shortest possible period of bed rest, so that inactivity and loss of muscle strength are limited.

Recovery

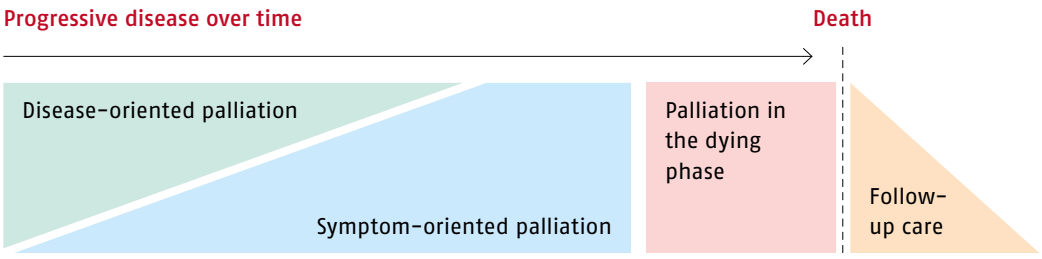
There is convincing evidence that physical activity after the end of cancer treatment has positive effects on the patient's physical and mental health. Summaries of various randomized studies have demonstrated that physical activity and exercise interventions can lead to gains in physical functions, decreased symptoms and increased quality of life (Buffart 2017; Sweegers 2018). Exercise interventions are also generally most effective in this phase when they take place under guidance. Within the scope of healthcare, exercise interventions after the end of treatment aim to optimise the patient's exercise capacity to the extent necessary to achieve personal life goals in relation to daily activities, work and sports. Exercise interventions can also be aimed in a more general sense at resuming or developing an active lifestyle and removing barriers to or facilitating exercise. Exercise interventions after the end of treatment can be classified as healthcare if there is a therapeutic goal.
Important components of exercise interventions are:

- shifting and/or learning how to deal with boundaries;
- obtaining/increasing confidence in one's body;
- increasing one's enjoyment of exercise;
- developing or regaining an active lifestyle;
- improving the physical functions and anatomical characteristics that are a condition for exercise insofar as the patient cannot do this (safely) independently;
- establishing conditions (knowledge, skills, perceived competency) for independently increasing/maintaining the desired level of physical functioning.

Which components apply and where the emphasis of the healthcare lies is determined by the therapist in consultation with the patient. The type of exercise intervention should be aligned with the patient's personal wishes and goals and the baseline situation. In this context, the baseline situation means the existing dysfunction in functioning and anatomical characteristics, existing limitations in activities, available room for adaptation, the behaviour and the perceived barriers to exercise. The therapist will base the choice of individual activities and the load level on the individual patient; in other words, the provided healthcare is customised.
In general, it can be said that the motivation for activities is greatest when the activity is offered at the right competency level of the patient (challenging but not too difficult) and if the activity leads to greater autonomy and social connectedness.

Metastatic disease

With most forms of cancer, the presence of distant metastases means that a cure is no longer possible and that the patient is in the palliative phase of the disease from that moment on. However, this does not always mean that the patient will die soon. From that moment on, the treatment is no longer focused on eliminating the disease but rather on holding the disease at bay for as long as possible, delaying and combating complaints and symptoms, promoting the quality of life and daily functioning and sometimes also on extending life. In the spectrum of palliative care, the following figure provides an overview of the various stages of palliative care (IKNL 2017).



The spectrum of palliative care (IKNL 2017)

With some types of cancer a cure is still possible even though there are distant metastases. Exercise interventions in the presence of metastatic disease comprise a promising strategy for optimising functional capacity, independence and quality of life (Dittus 2017). Physical activity can help prevent or delay decline in endurance and muscle strength. This way, an adequate physical function for performing activities of daily life can be maintained. Physical activity can help the patient maintain and/or increase his/her functional status, an important factor in the decision-making process of medical treatment. This stresses how important it is to decrease the decline in physical function and quality of life. Exercise interventions within the scope of healthcare (i.e. under the guidance of a physical therapist or exercise therapist) as part of palliative care are recommended if there is a therapeutic objective or if there are safety risks in relation to exercise and load. PRACTICE GUIDELINE

Note A.5 Organisation of healthcare

When offering an exercise intervention, it is important for the therapist to immerse him/herself in cancer-specific guidelines. The therapist focuses on the side effects and the possible effects of the medical treatment of cancer on (movement-related) functioning, and on the safe handling of these effects when conducting the exercise intervention.
Due to the life-threatening character of cancer, patients often experience illness-related anxiety or stress (either realistic or not); if this anxiety and stress interfere with the treatment, the therapist will also have to handle this in an appropriate manner. It should be clear that patients often have complex disease processes that have major impacts on their functioning. In this context, this means there are biopsychosocial and spiritual issues; the whole person is affected by the illness and its consequences. The therapist plays an important role in this complexity. The roles of the therapist and the associated challenges can be categorised as follows.

The therapist as a professional

As a professional, the therapist meets the minimum requirements defined by the professional groups to be competent and authorised and based on this to conduct an assessment of the demand for healthcare put to him/her. The physical therapist and exercise therapist work in a very dynamic medical field of increasingly improving diagnostics, personalised treatment forms, scientific substantiation and enhancement of knowledge about the (latent) consequences of the illness and its treatment. All of this requires therapists to not only practice their profession but to

continuously learn as well. (Self) education and differentiation are experiencing strong growth. In addition, the increasing tumour-specific expertise is creating new challenges for the professional groups, such as the question of whether one can still work in the field of oncology as a specialised generalist or if (sub)specialisations have to be developed.
In recent years, many steps have been taken with regard to scientific substantiation of movement-related functioning in conjunction with oncology. Unfortunately, an evidence-based solution is not yet available for all problems. It is up to the professional to properly translate the knowledge so that the position of an exercise intervention is granted a recognised position – which is above all also understood by others – in the continuum of oncological care.

The relationship with the patient

As a professional, one is confronted with patients who have been diagnosed with cancer and have a demand for healthcare regarding movement-related functioning. Many aspects play a role in the continuum of oncological care. First and foremost is the diagnosis, whereby the phase of the illness and its extensiveness and prognosis can lead to a large degree of uncertainty, doubts, emotions and worries. During the process of guidance and advice, it's almost impossible for relationships not to become deeper. If the guidance takes place during a period of medical-therapeutic treatments, then chemotherapy, radiation and immunotherapy will always – possibly only in the short term – have an impact on the patient's physical capabilities. These responses can be reinforced by the individual patient's history. Every phase hence has its distinctive features with large individual variation.
Often the physical therapy or exercise therapy treatment doesn't start until after the medical treatment has ended and the patient runs up against the effects of the medical-therapeutic activities. Within prehabilitation, the therapist and patient meet when things are still going relatively well, leading to a different conversation and better insight into who each other is. The fact that one in three people is confronted with cancer either as a direct or indirect reality also applies to the professional. Human experiences with suffering from cancer make a deep personal impression. It is up to the professional to be aware of his/her own life experiences and with respect to the patient keep sight of his/her professional involvement while keeping the correct distance.

Collaboration with colleagues

Due to the complexity of the disease, it is desirable for numerous reasons for the professional to work together with colleague therapists; for the continuity of exercise care in one's own work environment and across disciplines. This is shaped by sharing experience and expertise, optimising treatment quality and promoting the expertise of other healthcare providers involved in oncological care. Collaboration is also needed in order to enable smooth patient transitions, thereby unburdening the patient, but also in order to keep sight of one's own competencies and on what working in oncological care means for the professional as a person.
In his/her analysis of each individual patient, the therapist will seek the best possible answer to the patient's demand for healthcare. It is inevitable for aspects to come to light that have a direct or indirect impact on movement-related functioning that are not within the scope of the need for assistance. The therapist determines the limits of the therapeutic possibilities (both specific to the profession and his/her own) within the processional competencies and, together with the patient, examines whether there are questions that do not belong to the physical therapy or exercise therapy domain and that consequently can be posed (and answered) better elsewhere.

Based on training and experience, but also on knowledge of the larger whole of the oncological care, each individual healthcare professional will make an informed decision. Having knowledge of and access to a network can help when it comes to offering the most optimal healthcare. This requires additional effort on the part of the professional, including effort that is outside the scope of his/her professional group. This effort makes a substantive contribution to the quality of professional activities.

Support of healthcare processes in the area of moving

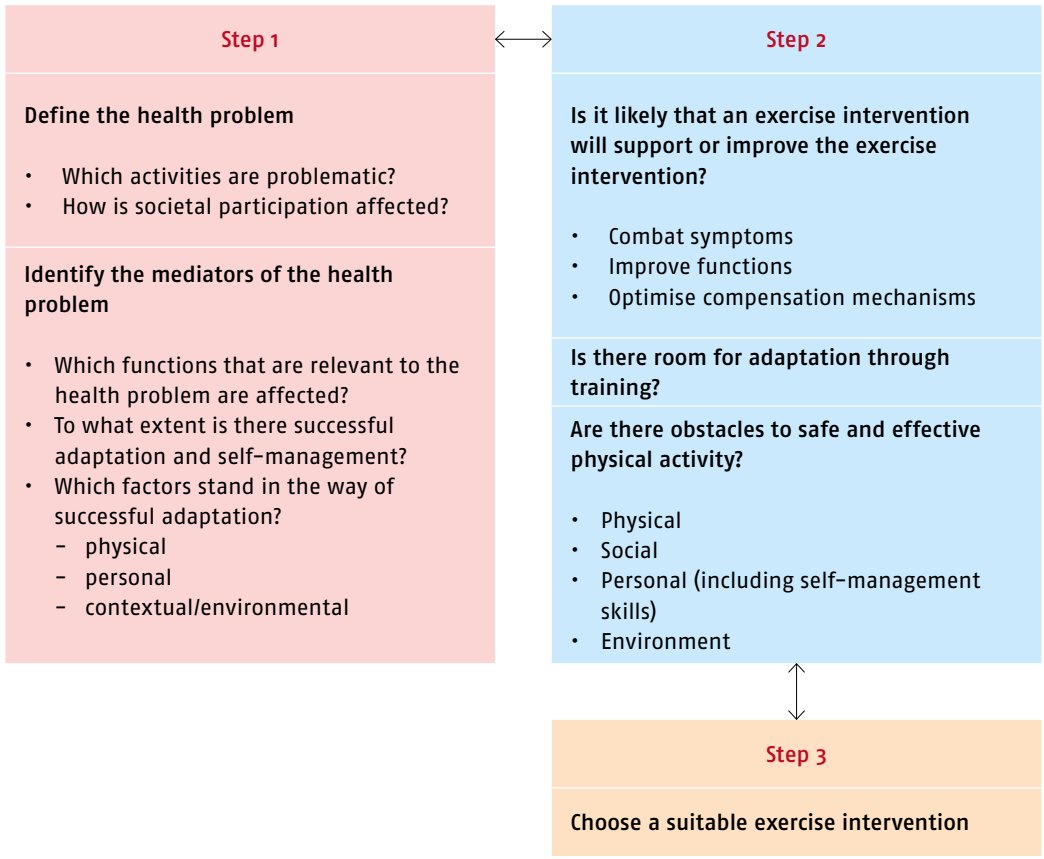
One of the characteristics of physical therapy and exercise therapy in oncological care is that they support healthcare processes in the area of moving. The therapy is aimed at guiding the patient towards a more active lifestyle. To ensure the patient exercises in a proper and responsible manner, it is important for the therapist to individually assess the oncological patient's capabilities and limitations with respect to mobility, muscle strength, posture and condition, quality of life, fulfilment and participation in society. In doing so, the therapist takes into account the goals set by the individual patient.
The goal of physical therapy and exercise therapy is for the patient to be able to continue with this improved lifestyle even after the end of the therapeutic intervention. The therapist is involved with movement-related functioning in terms of prevention, guidance, treatment and training. The therapist's role is to coach the patient in discovering the many different ways of moving and increasing the repertoire of postures and exercise strategies.

Complexity of healthcare

The 'Physical therapy in oncology domain description' (NVFL 2017) includes an overview that helps assess the patient's need for healthcare based on the complexity of the problems. It is important for a therapist to be conscious of his/her own skills and refer the patient in a timely manner, when necessary. This also applies to referrals to other possibly relevant specialties in physical therapy, such as geriatrics, psychosomatic or pelvic floor physical therapy. The general principle of 'unskilled is unauthorised' applies here. PRACTICE GUIDELINE ^

Note B.1 Choice of exercise intervention

In order to determine whether exercise intervention is indicated and what the most suitable exercise intervention is for the individual patient, the guideline panel opted to follow the step-by-step plan described by Stuiver (2020).
Step 1 consists of determining the need for assistance and the factors associated with the need for assistance. In step 2 a determination is made as to whether these factors can be positively impacted with an exercise intervention and how much room there is for change (adaptation). To this end, the individual patient's capacity and barriers with respect to exercise (either independently or supervised) are assessed. Based on these considerations, the most suitable approach is chosen in step 3. A periodic review is done to see whether support with the chosen exercise intervention is still fitting for the patient's situation and whether there is still an indication for guidance within the healthcare. The various steps are, of course, gone through in a shared decision-making process with the patient.

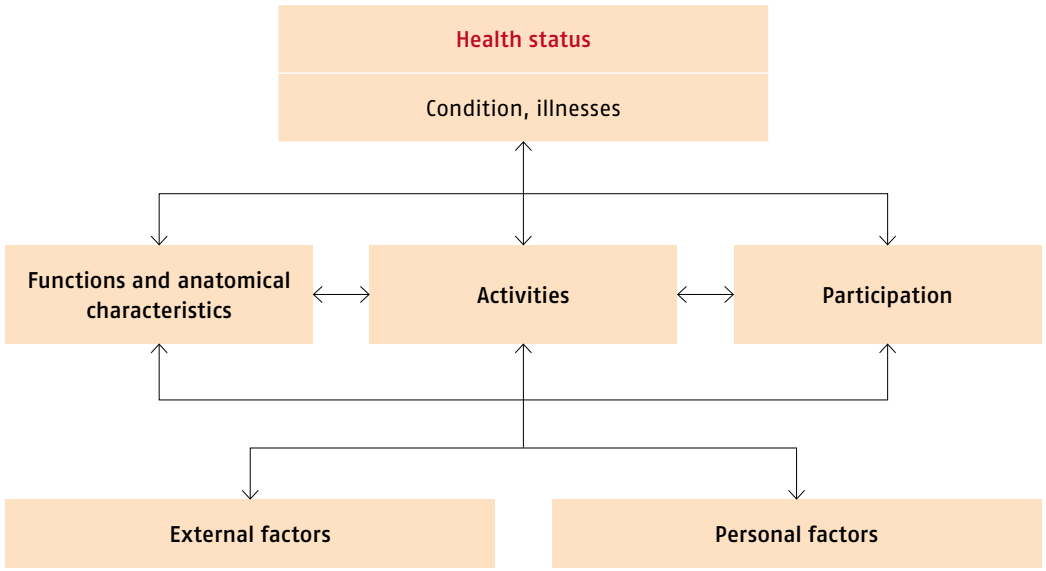


Three-step plan for choosing the most suitable exercise intervention. Source: Stuiver 2020

Step 1: Identification of the need for assistance

The goal of the intake (taking of the medical history and physical examination) is to determine which factors are related to the need for assistance). These factors are called mediators.
A useful concept for identifying the mediators of a health problem and the need for assistance stemming from this is the model of the 'International Classification of Functioning, Disability and Health' (ICF) (WHO 2001). See the figure on the following page.

The ICF model describes how people function, including the factors that may impact that functioning. For example, someone's health can be described at the level of bodily functions and anatomical characteristics, at the level of activities and at the level of participation. The model also has factors at the environmental level, called external factors in the model, and at the personal level, the so-called personal factors that can affect someone's functioning.
At the level of activities and participation, a differentiation can be made between the capacity (that which an individual is able to do, under standardised circumstances) and the performance (that which an individual does in daily functioning).
Mediators can occur at all ICF levels, including environmental factors and personal factors. If, when identifying the need for assistance, mediators come to light that might be influenced by exercise, an exercise intervention can be considered.



International Classification of Functioning, Disability and Health (ICF); classification that can be used to describe a person's functioning (WHO 2001)

Step 2: Ability to adapt

During this step it is determined whether an exercise intervention is a suitable intervention for influencing the mediators of the health problem. An exercise intervention can be considered as a sum of interventions that is aimed at improving the performance of physical activities. These interventions hence entail information provision and training, but also interventions that are aimed at behavioural change.

The most suitable intervention is determined by evaluating the individual's current capacity and performance, by examining how the capacity or performance can be improved and by identifying which factors hinder or promote this improvement. When it is determined that an exercise intervention is a suitable intervention, it is important to determine whether the patient can move independently safely and effectively. This means that the conditions for effective training stimuli (clinical status) are evaluated on the one hand, but also self-management skills on the other hand. Barriers can concern mental, emotional, social, personal or environmental factors. The social environment can play an important role in a patient intending to develop (new) behaviour. The loved ones of people who are living with or after cancer can play an important role in the degree to which an individual is challenged or inhibited when it comes to exercising.

Step 3: Choosing a suitable exercise intervention

The presence of barriers for safe and/or effective independent exercise is an indication for starting an exercise me guided by a physical therapist or exercise therapist.

If a physical therapy or exercise therapy exercise intervention is indicated, a specific intake is done. The first part of this is a conversation in which the patient's wishes and goals are identified. Based on exclusion criteria, the therapist determines whether the patient can exercise safely. Exclusion criteria can consist of complaints and symptoms that impede effective and safe exercise or entail serious physical risks based on the treatment or present co-morbidity.

(Interim) exclusion can be a reason for consultation with the medical specialist, conducting an exertion diagnosis or a referral to a specialised physical therapist, GP, rehabilitation physician or psychosocial healthcare provider.
Regardless of the phase of the illness/treatment in which the patient is, the guidance can consist of the following components: 1) exercise encouragement and advice, 2) optimisation of the activities relevant for the patient and optimisation and maintenance of the functions and anatomical characteristics that are a condition for exercising, 3) combating complaints during exercise and combating barriers to exercising and 4) promoting behavioural change with regard to an active lifestyle.
The concrete content of the exercise intervention is determined by the treatment phase, the patient's individual goals and wishes, the capacity level (both physical as well as mental/emotional), the degree of trainability, and the patient's behaviour and preferences for training tools. When determining the content of the exercise intervention it can be of added value to differentiate between treatable quantities and treatment goals. A treatment goal is something you work towards, such as work resumption, developing or maintaining an active lifestyle or independently carrying out general activities of daily life (ADL). Based on the treatment goal, the therapist can examine where someone gets stuck or what is difficult. The activities, functions or factors that impact functioning are treatable quantities. The treatment goal can be a function or complaint that can be evaluated with the PSC, for example; a treatable quantity can be evaluated with a measurement instrument in most cases.
Possible treatable quantities are:

- increasing the maximum aerobic endurance (capacity);
- increasing the strength of local muscle groups muscle and the muscle endurance;
- increasing flexibility (within the framework of scar tissue and muscle and/or joint stiffness);
- improving body composition, posture and the manner of movement and exercising and improving coordination and balance;
- increasing insight into load and capacity;
- decreasing fear of movement;
- gaining a positive (affective and instrumental) attitude and the intention to have an active lifestyle.

The exercise intervention is configured so that improvements of basic motor skills are aligned as best possible with the activities for which they are deemed conditional. In addition to training at the functional level (basic motor skills), attention is also paid to the activity level (skill, action and movement strategy and variation in these strategies). The (partial) skills required for performing activities can be improved with functional training. Functional training is ideally suited for integrating the effects of training into daily life. PRACTICE GUIDELINE ^

Note B.2 Training recommendations

Physical activity for people living with or after cancer is generally safe. There is sufficient evidence to be able to conclude that endurance and/or strength training in people living with or after cancer can improve general health, physical functioning and quality of life, as well as decrease anxiety, symptoms of depression and fatigue (Buffart 2017; Campbell 2019; Van Vulpen 2020).
The FITT principles are specified for each health outcome in the following table (Campbell 2019). These FITT principles have proven effective for patients who can handle this level.

Exercise recommendations which have proven effective for patients for whom this level is achievable (Campbell 2019)

Health outcome	Aerobic training	Strength training	Aerobic training + strength training
Fatigue	3x/week, 30 min/ session at moderate intensity	2x/week, 2 sets of 12–15 reps at moderate intensity	3x/week, 30 min/session moderate intensity aerobic training in combination with strength training of the large muscle groups in 2 sets of 12–15 reps at moderate intensity
Quality of life	2–3x/week, 30–60 min/ session at moderate to high intensity	2x/week, 2 sets of 8–15 reps at moderate to high intensity	2–3x/week, 20–30 min/session moderate intensity aerobic training in combination with 2x/week strength training of the large muscle groups in 2 sets of 8–15 reps at moderate to high intensity
Physical functioning	3x/week, 30–60 min/ session at moderate to high intensity	2–3x/week, 2 sets of 8–12 reps at moderate to high intensity	3x/week, 20–40 min/session moderate to high intensity aerobic training in combination with 2–3x/ week strength training of the large muscle groups in 2 sets of 8–12 reps at moderate to high intensity
Anxiety	3x/week, 30–60 min/ session at moderate to high intensity	insufficient evidence	2–3x/week, 20–40 min/session moderate to high intensity aerobic training in combination with 2x/ week strength training of the large muscle groups in 2 sets of 8–12 reps at moderate to high intensity
Depression	3x/week, 30–60 min/ session at moderate to high intensity	insufficient evidence	2–3x/week, 20–40 min/session moderate to high intensity aerobic training in combination with 2x/ week strength training of the large muscle groups in 2 sets of 8–12 reps at moderate to high intensity
Lymphoedema	insufficient evidence	2–3x/week progressive strength training of the large muscle groups does not exacerbate lymphoedema	insufficient evidence
Bone health	3–5x/week, 30–60 min/ session at moderate to high intensity	2–3x/week strength training and/or impact training	3–5x/week, 30–60 min/session moderate to high intensity aerobic training in combination with 2–3x/ week strength training and/or impact training
Sleep	3–4x/week, 30–40 min/ session at moderate intensity	insufficient evidence	insufficient evidence

Moderate intensity: 40–59% of the heart rate reserve or VO_2reserve, high intensity: 60–89% of the heart rate reserve or VO_2reserve

The therapist can set training parameters based on the recommendations regarding exercise with cancer, personal goals, clinical state and circumstances of the patients (which also includes the patient's capacity to adapt to changing circumstances). However, when interpreting and applying recommendations it is important to keep in mind that proof is often based on research with a limited number of cancer types (e.g. breast cancer). Moreover, research is often not aimed at patients with a very bad initial endurance or low muscle strength.
There are indications in scientific literature that the effects of certain interventions are greater in patients with the greatest need for improvement of physical fitness and decrease of fatigue (Buffart 2018). These patients may not initially be able to stick with the recommended FITT principles. The therapist therefore plays an important role when it comes to advising, supporting and motivating the patient and working towards the training parameters and the desired load level.
To achieve the main training effects, a training intensity is needed whereby the heart and circulation are working at least at a level of 50 to 60% of the VO_2max or 70 to 75% of the maximum heart rate. It is therefore preferable for aerobic training to be dosed based on the VO_2max or the maximum heart rate and heart rate reserve. The heart rate reserve is determined by subtracting the resting heart rate from the maximum heart rate. The optimal training intensity can be calculated using the Karvonen formula.

The Karvonen formula

Training heart rate = resting heart rate + (desired % of load x heart rate reserve)

When determining the training intensity, the therapist takes into account the side effects or symptoms of the disease or treatment that impact the patient's capacity. The recommendation is to base the training intensity – next to valid and reliable exertion tests – on physiological parameters (heart rate, clinical symptoms of exertion) and the perceived exertion level during the training. For the latter, the Borg Rating of Perceived Exhaustion (RPE) scale (6–20) is a suitable tool. This scale is used by the patient to indicate the degree to which an activity or test is perceived as strenuous.
Strength training for people living with or after cancer is primarily described in combination with aerobic training in the literature. From the physiological standpoint, it seems plausible that adding strength and endurance training helps increase aerobic capacity. Because strength training is part of the general exercise guidelines for people living with or after cancer, it will often be desirable to also have strength training be a part of an exercise intervention.
A classic strength training session is circuit training for 8 to 10 large muscle groups of the lower and upper extremities and the torso. The following phases can be differentiated in the building of strength training:

- the adaptation phase, when the patient learns the coordination of the exercise and then becomes familiar with the exercise and the load;
- the endurance phase, when the number of reps and weight used is gradually increased;
- the hypertrophy strength phase, when the diameter of the individual muscle fibres increases and there is an increase of the quantity and strength of the connective tissue.

During the adaptation phase, a low load (<50% 1RM) is used with 5 to 10 reps. Here the accent is on learning to correctly perform the exercise. During the endurance phase, the load is increased to 50 to 60% of the 1RM with 10 to 15 reps, or more if this is desirable. During the hypertrophy strength phase, 6 reps (85% 1RM) to 12 reps (65% 1RM) can be used. For increasing strength, training with a higher percentage of the 1RM (and hence fewer reps per set) is more effective than training with lower resistance. To achieve hypertrophy, the resistance is of lesser importance, as long as the patient exercises until local exhaustion (Lopez 2020). PRACTICE GUIDELINE

Note B.3 Measurement instruments

Measurement instruments suitable for oncological problems. Source: KNGF 2011; VRA 2017

		Measurement instrument
problem	detection	• Load meter • Patient-Specific Complaints (PSC)
	activities and participation	• Patient-Specific Goal-setting method (PSG)
(health-related) quality of life	(health-related) quality of life	• European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – C30 or SF/RAND-36
physical functions	physical functioning	• European Organisation for Research and Treatment for Cancer Quality of Life Questionnaire (EORTC QLQ-C30) • 36-Item Short Form Health Survey (SF-36 / MOS SF-36 / RAND-36)
	activity level	• Specific Activity Scale (SAS) • Physician-based Assessment and Counselling for Exercise (PACE)
functions and anatomical characteristics	fatigue	• Multidimensional Fatigue Inventory (MFI)
	sleep	• Sleep scale of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – C30
	pain	• Visual Analogue Scale (VAS) pain • Numeric Rating Scale (NRS) / Verbal Rating Scale (VRS) • European Organisation for Research and Treatment for Cancer Quality of Life Questionnaire (EORTC QLQ-C30) • 36-Item Short Form Health Survey (SF-36 / MOS SF-36 / RAND-36)
	exercise capacity	• Maximal exertion test with respiratory gas analysis • Six Minute Walk Test (6MWT) • Steep Ramp Test • Borg RPE scale • One-Repetition Maximum (1RM)

functions and anatomical characteristics (continuation)	balance	• Timed Up and GO (TUG) • Fullerton Advanced Balance (FAB) scale
	body composition	• Body Mass Index (BMI) • Abdominal girth • Bioimpedance analysis/spectroscopy (BIA/BIS)
personal factors	anxiety	• Hospital Anxiety and Depression Scale (HADS) • Center for Epidemiology Depression (CES-D)

* Most of the measurement instruments mentioned here are available at www.meetinstrumentenzorg.nl.

PRACTICE GUIDELINE

Note B.4 Personalised guidance

When there are complaints or problems due to the illness or treatment of cancer, it may be necessary to adapt the exercise intervention ('complicating factors'). Dekker (2016) describes a strategy for adapting an exercise intervention to the presence of co-morbidity. This strategy was then also used for adapting the exercise interventions for patients with breast cancer or ovarian cancer with other forms of co-morbidity (Stelten 2020; Van der Leeden 2018). Specific recommendations have been compiled for a number of complicating factors in this guideline. In addition, there are possible points of attention stemming from the treatment of cancer that are relevant to shaping the exercise programme. These are discussed below.

Lymphoedema

There is strong evidence that physical activity does not increase the risk of developing lymphoedema in breast cancer patients (Campbell 2019) and moderate to strong evidence that physical activity can decrease symptoms related to lymphoedema (Nelson 2016). Strength training in particular may have a positive effect on decreasing symptoms of lymphoedema (Hasenoehrl 2020). In women who have had surgery for a gynaecological tumour, strength training may have positive effects on physical functioning, fatigue and strength, without affecting the status of the oedema (Do 2017).

The presence or risk of lymphoedema is in and of itself not an indication for strength training supervision by a therapist; the strength training can also be safely supervised by a trainer/coach. Physical therapy or exercise therapy is only indicated during the initial acute phase, when there is a therapeutic objective or a specific risk (e.g. with exacerbation of oedema, limited range of motion, pain that hinders the training and which the patient is not able to deal with very well on his/her own, or fear of movement).

Exertion does not have a negative impact on the arm volume or the severity of symptoms. Although there are indications that strength training even with higher resistances is safe for people with lymphoedema of the upper extremities (Cormie 2013), the general recommendation is to start with low resistance and gradually increase it. The emphasis is on shifting the weight through the entire range of movement and maintaining the correct posture. Here the therapist continuously monitors the symptoms and complaints of lymphoedema. The Lymphoedema Guideline states that staying active and aiming to get enough exercise helps prevent lymphoedema (NVDV 2014).

Bone health

Women can reach menopause earlier due to cancer treatment, which is associated with an increased risk of osteoporosis. Decreased bone density (osteopenia) and an increased risk of fractures have been described for breast cancer in particular (Chen 2005). Men can also experience decreased bone mass due to antihormonal treatment. The evidence of the effectiveness of exercise on bone health is contradictory. Moderate to high intensity endurance training in combination with strength training and impact training, for 30 to 60 minutes per session two to three days per week may have positive effects on bone health in patients with breast or prostate cancer (Schwartz 2020).

Training programmes without an impact component likely have too little of an effect on bone health. Patients with osteoporosis have a contraindication for exercise with an excessively high load at vulnerable locations. It may be unsafe to prescribe taxing exercises for the bones for people with osteoporosis. People with joint, orthopaedic or stability problems will benefit more from an exercise intervention aimed at reducing their risk of falling.

The bone health can also be affected by the disease itself, in the form of bone metastasis. Bone metastasis occurs most frequently in patients with multiple myeloma, prostate cancer, breast cancer and lung cancer (D'Oronzo 2019). Bone pain and a high incidence of fractures contribute to a bad presentation status and decreased quality of life (Aielli 2019). Research has shown that (strength) training is possible without serious side effects. Depending on the location of the bone metastasis, it is important for the therapist to adapt a training intervention so that the patient can train safely (Cormie 2014). Section C.1 'Bone Metastasis' comprehensively describes the safe administration of exercise interventions in patients with bone metastasis.

Body composition

The negative changes in body composition associated with (the treatment of) cancer can result in a need for assistance on the patient's part with regard to weight gain or maintenance (with the goal being to increase the fat-free mass) or weight loss (through decreasing the fat mass). Sarcopenia, loss of both muscle mass and function, can occur with various types of cancer (Baracos 2018). With cachexia there is decreased muscle mass and unintended weight loss, often caused by malnutrition during illness. Cachexia occurs more frequently in people with lung, colon and pancreatic cancer, with a bad prognosis and with advanced-stage cancer (Carson 2013).

The body composition can be improved with training. Moderate intensity aerobic activities and combined (moderate intensity) aerobic training and strength training have beneficial effects on the body composition (Courneya 2007). An intervention aimed at improving body composition (increased fat-free mass) may also have beneficial effects on patients with metastatic disease. An association has been found between the muscle index (calculated as the muscle mass on a CT scan corrected for height) and fatigue in male patients during treatment with chemotherapy in the palliative phase (Neefjes 2017).

Physical activity costs energy, and the amount of energy consumption depends on the duration, intensity and type and frequency of the activity, as well as the patient's body composition and weight. Proteins play a particularly important role in maintaining and building muscle mass. It is also important that carbohydrates be used after moderate to high intensity physical activity, so that the proteins are effectively absorbed and are available for muscle building. In addition, vitamin D supplementation can positively influence the muscle strength and function (Halfon 2015). It is recommended that patients living with or after cancer be regularly screened for the need for healthcare for sufficient and complete nutrition (Muscaritoli 2021). The risk of malnutrition can be

assessed with the help of the Patient Generated-Subjective Global Assessment (PG-SGA; complete version). If (a risk of) malnutrition is detected, the therapist will refer the patient to a dietician. An adequate nutritional condition and food intake are preconditions for effective building of muscle mass and function. It may therefore be relevant to also involve a dietician in the treatment of patients who do not have (a risk of) malnutrition. In particular when improving body composition or weight loss is an important goal for the patient, consultation with a dietician is important because the dietician can give targeted advice about any adaptations in the patient's diet. Adapting the diet of people living with or after cancer is complex and can necessitate the involvement of a specialised oncology dietician. The therapist can also make the patient aware of the website voedingenkankerinfo.nl. More detailed information for physical therapists and exercise therapists can be found in the *Handboek Voeding en Kanker (Nutrition and Cancer Handbook)* (Vogel 2016).

Posture and safely and effectively performing exercises

The way in which exercises are performed is essential for ensuring effective training. Incorrectly performing an exercise can cause unnecessary complaints and hence discourage the patient. For all patients, but especially for patients with impairments, it is therefore important to carefully analyse how the patient exercises, how effective this exercising is and whether the manner of exercising is causing or perpetuating any current complaints or may cause complaints in the future. It is the therapist's task to ensure the patient becomes aware of his/her manner of exercising (with the help of a mirror, if need be). The patient also receives a clear explanation about which (im)possibilities exist in the physical realm. Becoming aware is a learning process in which the therapist helps the patient – including in daily life – to exercise in a better and more functional manner with existing physical limitations.

Cognitive functioning and emotional wellbeing

The impact of the illness on the patient's mental/emotional wellbeing depends on the type of cancer, the type of treatment, the dose and duration of the treatments, the patient's coping and the patient's environment. Patients can deal with anxiety and processing complaints, fatigue, a distorted body image or feelings of depression as a result of cancer. They can experience a loss of confidence in their own body. In the context of exercise intervention, the patient's emotional state can be an inhibiting factor to movement-related functioning. Cognitive dysfunctions occur frequently in patients. It is important for the therapist to make an assessment of any cognitive problems and align the information transfer with this.
Exercise may have a positive effect on a patient's cognitive functioning and emotional wellbeing (Campbell 2019; Husson 2015), but in some cases the patient needs mental/emotional oncological healthcare or support (available through the psychosomatic, psychomotor or oncology physical therapist or by means of multidisciplinary specialised rehabilitation). Specific problems may remain undetected because the patient does not communicate the complaints or does not recognise the complaints as such. The patient's need for healthcare can be identified using detection tools.
For more information, consult the Detecting the Need for Psychosocial Healthcare (Detecteren behoefte psychosociale zorg) guideline by the Dutch Society of Psychosocial Oncology (NVPO 2017).

Vulnerability

Cancer and the treatment of cancer can lead to increased vulnerability. Vulnerability can manifest itself in a deterioration of various physiological systems, resulting in unintended weight loss, decreased endurance, general weakness, a slower walking pace and low degree of physical

activity. Vulnerability occurs frequently in the elderly and in patients with a lot of co-morbidity. Vulnerable elderly people are at an increased risk of hospitalisation, poor mobility and death (Fried 2001; Gill 2010). Physical problems such as neuropathy, sarcopenia, muscle weakness and fatigue can be comparable to those in elderly people without cancer. Cancer treatment can exacerbate existing problems, accelerate deterioration and cause younger patients to develop problems that typically do not occur at a younger age (Maccormick 2006). The exercise tolerance can therefore be lower than is expected for a certain age group.
Because inactivity is a part of vulnerability and impacts components of vulnerability, an exercise intervention can be a strategy for tackling complaints. Guidance by a therapist and encouragement of an active lifestyle can help prevent or decrease problems associated with vulnerability (Schwartz, 2020). In addition, patients can also exhibit or experience vulnerability in a domain other than the physical domain. Experiencing the disease of cancer and its treatment has a big impact on daily life, life expectancy and societal role changes and gives rise to existential questions and uncertainties that can affect physical functioning. That is why vulnerability deserves the full and widespread attention of physical therapists and exercise therapists.
It is important for the therapist to detect signs early on that are in the social, mental/emotional, behavioural and existential domain, to name these and, in consultation with the patient and the referrer, to involve other experts (e.g. geriatric physical therapist, clinical geriatrician or geriatric specialist) as co-practitioners, if necessary (KNGF 2014). PRACTICE GUIDELINE ^

Note B.5 The safety of exercise interventions

Scientific research has shown that the risk of serious side effects due to physical activity in people who are living with or after cancer is low (<5%), and no life-threatening situations or fatalities have occurred (Speck 2010; Stout 2017). The number of patients that refrains from an exercise intervention after initial participation is also low (<10%) and the therapy compliance is generally high (>80%) (Singh 2018, 2020). It is, however, expedient to view research findings in the light of the limitations of conducting research. Patients who are involved in research on the effectiveness of exercise interventions are often more motivated, younger and more physically active compared to the general population and they typically also have an earlier stage cancer. Furthermore, exclusion criteria for participating in the study may have been applied, such as the presence of specific treatment-related side effects, other chronic illnesses or co-morbidity. This makes it so that research findings about the safety and feasibility of exercise interventions cannot be generalised towards the entire population of people living with or after cancer.

Both the illness and the treatment of cancer can affect the safety of exercise interventions. In order to formulate an effective exercise intervention, it is important to assess any complaints and symptoms. The American College of Sports Medicine (ACSM) has formulated recommendations – based on the National Comprehensive Cancer Network (NCCN) Survivorship Guideline – for when medical approval is necessary (meaning: consent from a medical professional for an exercise intervention) and/or further evaluation by a medical professional (Campbell 2019; NCCN 2018). This risk assessment is included in the following table.

Risk assessment of complaints and symptoms (Campbell 2019; NCCN 2018)

Description of the patient	Recommendations
no co-morbidity	• no medical evaluation needed • follow the general exercise recommendations
peripheral neuropathy, arthritis/musculoskeletal problems, poor bone health (osteopenia or osteoporosis), lymphoedema	• prior medical evaluation recommended • adjust exercise intervention based on the assessment
lung or stomach operation, stoma, cardiopulmonary condition, ataxia, extreme fatigue, severe malnutrition, worsened/changed physical condition (i.e. exacerbation of lymphoedema), bone metastasis	• prior medical evaluation recommended • approval by a physician prior to the exercise intervention

For the therapist it is important within the scope of the exercise intervention to look into the possible side effects on the (movement-related) functioning of the combination of medications used by his/her patient, and on the safe handling of these effects when implementing the treatment plan during a cytostatics cure. For professionals who are involved in caring for patients who have been or are being treated with cytostatics, the Safe Handling of Cytostatics Manual (Handreiking veilig omgaan met cytostatica) is available (IKNL 2015). PRACTICE GUIDELINE

Note C.1 Bone metastasis

Reason

Bone metastasis can lead to pain, decreased physical functions and decreased functioning in the area of activities and participation. As a result, patients with bone metastasis can experience decreased quality of life. Sufficient physical activity can improve physical functioning and is recommended for people living with or after cancer. For patients with bone metastasis, an exercise intervention often remains unused due to uncertainty about the safety and the risk of side effects, such as pathological fractures. In order to support therapists, it is therefore important to formulate recommendations about the safe application of effective exercise interventions in the presence of bone metastasis.

Clinical question

What is a safe application of exercise interventions for patients with bone metastasis?

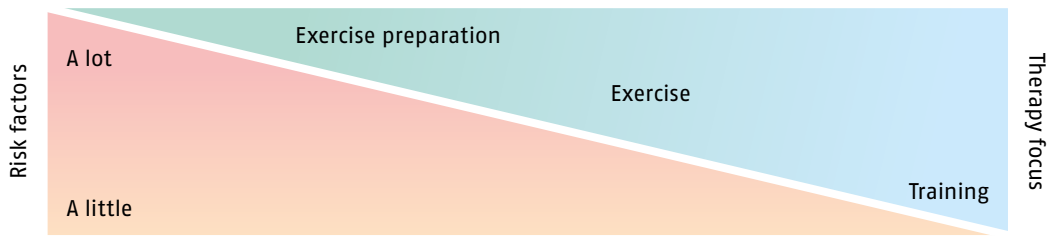
Literature

The literature states that exercise interventions for patients with stable bone metastasis do not have an increased risk of serious side effects as a result of an exercise intervention compared to no exercise intervention. Even participating in sports and games is associated with a very low risk of side effects which are related to exercise in the presence of stable bone metastasis.
However, patients with pain or unstable bone metastasis have not been included in a large part of the scientific studies, and consent from the treating physician, a comprehensive transfer with the patient's functional status or a minimum level of functioning was required prior to participation in an exercise intervention.

In the presence of bone metastasis, strength exercises were prescribed whereby the load in the area with the bone metastasis is minimised and/or resistance bands were used instead of devices. With these modifications, patients with bone metastasis still exhibited positive effects in various outcomes, such as physical functioning and muscle strength.

Considerations

When considering offering an exercise intervention to patients with bone metastasis, it is important to collect the correct background information. Patients with bone metastasis who see a therapist will have stable metastasis in most cases. In the event of doubt, it is important to verify this with the treating physician. The box below contains an overview of the possible risk factors. This list was compiled by an international guideline panel consisting of experts in the area of exercise with bone metastasis, based on a systematic review and consultation of stakeholders (Campbell 2022, Weller 2021). Based on these risk factors, the therapist can assess whether the focus of an exercise intervention should be primarily on exercise preparation (aimed at the correct, safe performance of the exercise), on exercise or on training. See the figure below.



Focus of an exercise intervention in relation to risk factors

Risk factors for exercise for patients with bone metastasis

Factors related to metastasis
- Osteolytic metastasis
- Metastasis in weight-bearing bones (femur, spine, pelvic ring, hip socket)
- Pain related to the location of the metastasis
- Neurological symptoms
- Use of pain medication related to the location of the metastasis

Factors related to the treatment of metastasis
- Irradiation of the metastasis in the past two months
- Planned or previous surgical or medical treatment for skeleton-related incidents or symptomatic conditions related to the skeleton

Factors related to (the treatment of) cancer
- Progression of the disease
- Metastasis in other organ systems (e.g. brains, lung)
- Cancer type that often manifests in osteolytic metastasis (such as lung, thyroid and renal cell carcinoma)
- Current use of medication that inhibits breakdown of bones or makes bones stronger (denosumab, zoledronic acid), or use for a period of >6 months

Patient-related factors
- General symptoms such as co-morbidity, fatigue, extreme weight loss
- No or little experience with physical activity
- Poor ECOG performance status
- Two or more falls experienced in the last 12 months
- Osteoporosis
- Impairments in ADL
- Cognitive dysfunction that makes complying with precautionary measures unreliable

ECOG = Eastern Cooperative Oncology Group.

In addition, in the case of metastasis in the long bones, a risk analysis can be generated with the help of the Mirels Classification (Howard 2018; Sheill 2018) and for metastasis in the spine with the Spinal Instability Neoplastic Score= (SINS; Fox 2017). However, these scores are not routinely used in all Dutch hospitals and are therefore not always available. Neurological symptoms are suspicious, and the therapist will always immediately refer a patient with neurological symptoms back to the physician for additional tests.
When setting up the exercise intervention, the therapist takes into account the location and type of bone metastasis in order to decrease the risk. If modifications are necessary, you can consider omitting certain exercises or tests, putting less load on a specific area or modifying the movement, exercise or test. Galvão (2011) developed a multimodal exercise intervention for patients with prostate cancer and bone metastasis in order to minimise the compression load on the areas with bone metastasis and take account of the decreased capacity of the bone. See the following table.

Multimodal exercise intervention for patients with prostate cancer and bone metastasis (Galvão 2011). **Note:** This schedule is based on what is certainly safe; the modifications are therefore not absolute contraindications.

Location of the bone metastasis	**Type of intervention**					
	Strength training			**Endurance training**		**Flexibility exercises**
	Upper extremities	**Torso**	**Lower extremities**	**Load with weights**	**Not burdensome**	**Static**
pelvis	+	√	√[b]		√	√
lumbar	√		√		√	√[c]
thoracic/ ribs	√[a]		√	√	√	√[c]
thigh	√	√	√[b]		√	√
all regions	√[a]		√[b]		√	√[c]

√ Target area of the training. [a] Elbow flexion/extension allowed, with the exception of shoulder flexion/extension/ abduction/adduction. [b] Knee flexion/extension allowed, with the exception of hip flexion/extension. [c] Exception of flexion/ extension/rotation of the spine.

The therapist should be guided as little as possible by impairments but must realise that certain exercises are associated with an increased risk, e.g. transverse forces at a location with demonstrated metastasis. Direct 1RM tests are not recommended. With stable bone metastasis, 12 RM tests are generally thought to be safe. One can also consider not performing any tests and determining the load pragmatically based on the perceived load and quality of execution of the exercise. It is therefore important for the therapist to conduct an analysis of the force transmission chain for each exercise, and how the affected region is taxed as a result (Guo 2020). Deviating exercise patterns due to fear of movement must be taken into account here. These can cause potential complaints in other areas. Keeping an exercise intervention from a patient can also indirectly lead to injury because inactivity can result in falling and an increased risk of fractures. Functional training is important for patients with bone metastasis. Functional training might decrease the risk of an exercise intervention because only one's own weight, gravity and functional weights are used which the patient would also use in daily life. The therapist encourages the patient to exercise and provides a good explanation about any risks and how these can be limited to the greatest extent possible. This includes adjusting the way in which the various exercises can be performed where necessary. Knowledge transfer between the therapist and patient about how and in which form exercise tasks are performed is important, as is communication between the involved healthcare providers amongst each other so that patients receive uniform advice, so as to be certain that all relevant information about the (capacity of) bone metastasis is known to all involved healthcare providers and to ensure that symptoms and signs that might be related to (exacerbation of) bone metastasis are detected on time.
In general, the risks of an exercise intervention in patients with stable bone metastasis are low, but these possible risks of fractures or compression of the spinal cord, as indicated by the physician, are discussed with the patient, explained and documented in the patient file. The therapist weighs these risks in consultation with the patient against the benefits of exercise and the risks of not exercising.
The scientific evidence about the safety and feasibility of exercise interventions in patients with unstable bone metastasis is limited. The guidance of patients with unstable bone metastasis differs from patient to patient and necessitates an extensive risk assessment and consultation with the involved healthcare providers.
When a patient with bone metastasis wants to train independently, the therapist must instruct the patient in safely performing the exercises. At some point and at some level, (periodic) supervision will be important. Depending on the patient's situation, the therapist will estimate how frequently the patient will be seen. PRACTICE GUIDELINE ^

Note C.2 Cardiotoxicity

Reason

The current therapies for cancer make survival of the illness possible in the long term. Although many patients are cured, many therapies have both short-term and long-term cardiotoxic effects. Therapy-related cardiotoxicity can be defined as symptoms and signs of heart failure after the start of the medical-therapeutic process. These symptoms affect the safety of exercise interventions. To help therapists make informed choices, it is important to formulate recommendations for the safe application of an exercise intervention for the patient with therapy-related cardiotoxicity.

Clinical question

What is a safe application of exercise interventions for patients with therapy-related cardiotoxicity?

Literature

There is little scientific evidence about the safety of exercise interventions for patients with therapy-related cardiotoxicity. Two randomised studies concluded that an aerobic exercise intervention may be safe for patients with treatment-related heart failure. The results of one study suggest that an exercise intervention is particularly safe for patients who are able to maintain an exercise intervention. However, whether or not side effects result in not being able to maintain the intervention cannot be assessed.

Considerations

Caution should be exercised when offering an exercise intervention to patients with therapy-related cardiotoxicity. It may be possible for patients with reduced cardiac capacity to perform aerobic training safely, especially patients who are able to maintain an exercise intervention. However, more side effects were discovered in the intervention group with an aerobic exercise intervention than in the control group in the research results that were found (Jones 2014). Here it is unclear whether these side effects occurred as a result of the intervention. The therapist will consider an exercise intervention in consultation with the patient, whereby it is discussed with the patient what the risks are and what gains the exercise intervention can yield. An article by the European Society of Cardiology (ESC) contains an overview of the most common heart problems after a medical-oncological treatment (Zamorano 2016).
A proper inventory of risk factors will help the therapist assess whether the intervention will result in major risks of side effects and cardiovascular events and assess whether these risks outweigh possible improvement of the patient's condition.
The literature describes arrhythmias, increased number of complaints or increased severity of the complaints as a side effect. The box below provides an overview of the risk factors.

Risk factors for decreased cardiac capacity (Henning 2017)

Medication-related risk factors
- High risk: anthracyclines (doxorubicin, mitoxantrone, epirubicin, daunorubicin and idarubicin), cyclophosphamide, ifosfamide, clofarabine
- Moderate risk: trastuzumab, pertuzumab, sunitinib, sorafenib, imatinib
- Low risk: bevacizumab, dasatinib, imatinib, lapatinib
- Sporadic risk: etoposide, rituximab, thalidomide

Patient-related risk factors
- Cardiomyopathy or heart failure
- Coronary disease and/or peripheral vascular disease
- Hypertension
- Diabetes
- Previous or simultaneous treatment with anthracycline
- Previous or simultaneous radiation of the thorax
- Age >65 years
- Being female

Both the American Heart Association (Gilchrist 2019) and the European Society of Cardiology (ESC; Pelliccia 2021) states that by measuring the maximal exercise capacity it is possible to devise a customised personal exercise intervention that is safe. Performing an exertion test gives you the opportunity to identify abnormal cardiovascular responses which otherwise don't occur during normal daily activities.
Cardio Pulmonary Exercise Testing (CPET) can be of added value for patients with limited physical capacity if no progress is made or if there are worries about the patient's capacity. The CPET request is made in consultation with the physician or general practitioner. The results of the maximal exertion test can be used to determine whether physical training can be applied safely, for identifying limiting factors and for making an informed choice between forms of therapy and the intensity of physical training (Campbell 2019).
In scientific research, a maximal exertion test was unable to fully cover the risk of possible side effects in patients living with or after cancer and who were diagnosed with heart failure. There is insufficient evidence that training based on the results of an exertion test is effective for reducing the risk of cardiovascular events as a result of exertion (Riebe 2015). In addition, performing a maximal exertion test can be an unnecessary hindrance for starting an exercise intervention. The risk of cardiovascular events is highest when inactive patients with a cardiovascular condition are physically active at high intensity. It is therefore of added value to assess: 1) the patient's current level of physical activity, 2) the presence of symptoms and/or known cardiovascular problems, and 3) the desired training intensity. A maximal exertion test can be considered based on risk factors for decreased cardiac capacity (see the 'Risk factors for decreased cardiac capacity' box). Based on the health screening of the American College of Sports Medicine and the criteria from the decision tree of the Medical Specialised Rehabilitation in Oncology guideline, a diagram was compiled to support the clinical decision-making process prior to an exercise intervention (see the Practice Guideline). The maximal exertion test does not need to be done if there is a clear clinical indication that the test result has no added value for the treatment process. For people with heart failure as a result of oncological treatment, the ejection fraction may provide important information about the patient's capacity. If the patient performs worse than expected, the therapist will look for the cause of this. Based on clinical expertise, if cardiac risks are suspected, the recommendation is to avoid great exertion of force and valsalva manoeuvres (forcefully 'detaining' the breath in order to increase intra-abdominal and intrathoracic pressure).
No extensive assessment of the capacity is required for endurance training at low intensity or flexibility exercises (Riebe 2018). If therapy-related cardiotoxicity makes implementing an exercise intervention difficult, then it is expedient to consult the KNGF Cardiac Rehabilitation guideline. Based on this guideline, the therapist will assess whether referral to a therapist with sufficient knowledge and skills in the area of heart failure is necessary. PRACTICE GUIDELINE ^

Note C.3 Chemotherapy-induced peripheral neuropathy

Reason

Treatment with chemotherapy can result in central (brain, brain stem and spinal cord) or peripheral (nerves running from the spinal cord to the limbs) nerve injury. Chemotherapy-induced peripheral neuropathy (CIPN) is a side effect of treatment with medications such as platinum derivatives, taxanes, vinca alkaloids, thalidomide and bortezomib. CIPN is the result of damage to the peripheral nerves and causes symptoms of numbness, tingling and/or pain in the hands and/or feet. It also causes reduced muscle function and problems with co-ordination, which have a

negative effect on proprioception and control of body posture. These, in turn, lead to a decreased quality of life, increased risk of falling and decreased physical functioning. CIPN occurs in 20 to 95% of patients with cancer, depending on the type of chemotherapy, the patient's demographic characteristics and co-morbid conditions, and can persist for years after the treatment has ended. An exercise intervention may decrease the CIPN complaints. When administering an exercise intervention, it is important for therapists to take into account sensory and motor impairments and take suitable safety measures. The formulation of recommendations can support therapists in the safe application of effective exercise interventions in the presence of CIPN.

Clinical question

How should an exercise intervention be modified for patients with CIPN?

Literature

Exercise interventions for CIPN appear to be effective and safe for patients who are already experiencing complaints. Several studies describe that an exercise intervention improves the quality of life, strength, balance and CIPN-induced symptoms. The most frequently applied interventions consist of a combination of endurance, strength and balance training. The studied exercise interventions lasted between 3 and 36 weeks, with 10 to 60 minutes per session, spread out across two, three, five or seven days per week at low to high intensity. The exercises were performed supervised and unsupervised. Based on the scientific evidence, it is difficult to formulate concrete recommendations about FITT principles due to variability in intervention duration and structure and the type of exercises that was applied.
Because the various types of interventions were not directly compared to each other in a single study, it is not possible to draw a definitive conclusion based on the scientific literature about the most effective exercise intervention for patients with CIPN. Based on the available scientific evidence, it is generally not necessary to make modifications to an exercise intervention for patients with CIPN.

Considerations

In practice, patients often don't come with a need for assistance that is primarily aimed at reducing neuropathy. Considerations regarding CIPN are mainly an issue when these complaints (possibly) affect the physical therapy or exercise therapy treatment and/or diagnosis. Because no systematic adjustments were reported in interventional studies on exercise with CIPN, there appears not to be a generally valid necessity for such adjustments. The therapist will hence adjust the exercise intervention on the basis of the individual patient's symptoms and complaints and to the extent that adjustments are needed in order to safely and effectively implement the intended exercise programme. The guidance of patients with CIPN therefore differs from patient to patient. Good guidance and explanation about performing the various exercises are important. The therapist always gives individual guidance before allowing the patient to switch to group training if applicable. It is important for the patient to be told that the primary goal of the exercise intervention is not to decrease complaints. This will prevent incorrect expectations. In the communication with the patient it is also important to be clear about the possible effects of the exercise intervention on symptoms and functional status. That's because in practice the exercise intervention is not used to decrease symptoms of neuropathy. However, the scientific literature does show predominantly positive effects on quality of life, strength, balance and the functional status. It is therefore important to always consider whether it is desirable to implement an exercise intervention for optimising exercise behaviour and balance.

Exercise interventions in patients with CIPN do not increase the risk of side effects compared to no exercise intervention, provided that the exercise intervention has been adjusted to the patient's decreased sensitivity and/or strength. The therapist is guided as little as possible by the patient's impairments but does need to be aware that certain exercises lead to an increased risk of balance problems, for example. Offering the exercises as much as possible in an ADL-focused manner will optimise the transfer of effects to daily life.
Withholding an exercise intervention from a patient with CIPN can indirectly lead to injury. For example, fear of movement resulting from CIPN can increase the risk of falling and decrease the mobility.
Communication between the involved healthcare providers is important in connection with early detection of CIPN; the therapist can contribute to toxicity monitoring in this way.
It is important for the therapist to be alert to signs of neuropathy complaints (Scheel 2014):

- tingling and prickling sensations;
- strange feeling in the hands and feet;
- disrupted tactile sense;
- decreased pain sensation or shooting pain;
- decreased sensitivity to temperature;
- numbness;
- weakness or reduced muscle strength or function;
- coordination problems.

Additionally, starting an exercise intervention early on can prevent fear of movement. Where necessary, the therapist can seek out collaboration with the occupational therapist if problems occur in daily functioning. If the patient experiences pain while walking, the therapist can seek out collaboration with a podiatrist for an adjustment of the patient's shoes. PRACTICE GUIDELINE ^

Note C.4 Fatigue

Reason

Fatigue is one of the most frequent complaints in people living with or after cancer. Fatigue complaints occur in 75 to 100% of patients and can persist for a long time after (successful) treatment has ended (Abrahams 2016; Bower 2014; Hofman 2007). Due to the negative impact of fatigue on resumption of work, daily activities and social contacts, fatigue has an important effect on the quality of life of people living with or after cancer. It is therefore important to decrease these fatigue complaints.
Fatigue can not only play a role in a need for assistance when it comes to movement-related functioning, but decreasing fatigue can also be a need for assistance in and of itself. In both cases, it is important for the therapist to know which forms of exercise interventions are supposedly most effective for reducing (or limiting) fatigue complaints.

Clinical question

What is the most suitable exercise intervention for decreasing cancer-related fatigue complaints?

Literature

There is strong evidence that exercise interventions are effective for decreasing fatigue complaints in people living with or after cancer. These effects are not dependent on the patient's demographic or clinical characteristics. The severity of fatigue complaints prior to an exercise intervention is an exception to this; it does appear to have an influence. Both during and after the treatment, the effects are greater in patients with severe fatigue complaints prior to an exercise intervention compared to patients who experience few fatigue complaints.
No difference in effectiveness was found between interventions that were offered during or after the cancer treatment, between interventions with different frequencies (range: 2–5 sessions per week) and session duration (range: 15–120 minutes per session) or between aerobic training and strength training. A dose-effect relationship with regard to the intensity of the intervention was not demonstrated. A supervised exercise intervention under the guidance of a therapist is more effective than an unsupervised exercise intervention. With a 12-week supervised exercise intervention a positive effect on fatigue can be expected. No difference in effectiveness was demonstrated on fatigue complaints between a moderate intensity aerobic exercise intervention and 'High Intensity Interval Training (HIIT). For fatigue complaints caused by anxiety and depression, pain, anaemia, sleep problems, medication and malnutrition, an exercise intervention may not have any positive effects on fatigue.

Considerations

The ACSM exercise guideline for people with cancer states that an exercise intervention lasting at least 12 weeks, 3 days per week of moderate intensity has significant beneficial effects on fatigue both during and after the cancer treatment. There is suggestive evidence that exercise recommendations of longer than 30 minutes per session for longer than 12 weeks result in a greater decrease of fatigue than exercise interventions of short duration (Campbell 2019). For daily clinical practice, this means that it is not advisable to implement an exercise intervention at low intensity for decreasing fatigue. Additionally, various studies have shown that performing HIIT is safe for patients with cancer-related fatigue (Piraux 2020). The effectiveness of HIIT in relation to other forms of training has not been sufficiently described. Regular evaluation of the intervention is warranted in order to maintain a balance between the patient's load and capacity.
For fatigue complaints caused by anxiety and depression, pain, anaemia, sleep problems, medication and malnutrition, an exercise intervention may not have any positive effects on fatigue. It is therefore important when taking the medical history to assess factors that perpetuate fatigue (including processing problems, fear of a relapse, dysfunctional cognitions, irregular circadian rhythm, overactivity or underactivity and unrealistic expectations from the patient's environment) (Blijenberg 2007). When one of these factors is present, a behavioural approach (e.g. cognitive behavioural therapy, psychological and/or psychosomatic counselling), sleep therapy, medication or a consult with a dietician may be more suitable for decreasing the fatigue complaints (NCCN 2018; Portenoy 1999). Combined supervision of an exercise intervention and a behavioural approach and/or the use of dietetics should be considered. When patients are already suffering from severe fatigue when they are diagnosed, a cognitive behavioural approach is especially effective (VRA 2018). The Medical Specialised Rehabilitation guideline can be consulted if there are related problems in which several healthcare providers play a role.
The therapist can explain, with the assistance of psychoeducation, that fatigue can be a logical result of the illness and its treatment. In addition, the therapist can offer support with the performance of daily activities. Here the therapist can also consider referring the patient to an

occupational therapist. Obtaining insight into the exercise that already takes place in the patient's daily schedule can be useful. Here it can be clarified to the patient that physical activity doesn't only take place in the therapeutic environment but also in daily life. Recommendations regarding incorporating exercise into the ADL is desirable. Some activities or tasks may take on a different form in order to encourage physical activity. In these recommendations, customisation is essential for setting realistic treatment goals and providing optimal guidance. Social support can be of added value. The therapist can take stock of the home environment and social support. The social environment can help create a routine, for example by walking children to school or setting up a regular walking or biking date with a friend or family member. When guiding or giving advice, it is important to take into account the patient's preferences and interests.

It is also essential to view the problem in terms of the wider picture. Fatigue is almost never a stand-alone problem. Patients often present with combined problems. This is why it is desirable to apply a multidimensional approach and combined supervision.

With regard to fatigue in the palliative phase, see the Fatigue in the Palliative Phase of Cancer guideline of the IKNL. PRACTICE GUIDELINE

Colophon

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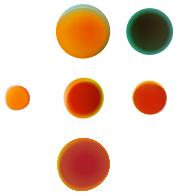
The KNGF aims to create the conditions in which high-quality physical therapy care can be provided that is accessible to the entire Dutch population, whilst recognising the professional expertise of the physical therapist.
The KNGF represents the professional, social and economic interests of over 18,000 registered physical therapists.



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