

DESK STUDY ON RECENT SCIENTIFIC EVIDENCE OF PA FOR CANCER PREVENTION FOR ADULTS AND SENIOR CITIZENS USED FOR CPPA (deliverable D2.1)

Contribution to WP2 - RESEARCH ACTIVITIES





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1. Abbreviations and Acronyms

BC Breast cancer

CIPN Chemotherapy-induced peripheral neuropathy

CPPA Cancer Prevention Physical Activity

CRF Cancer-related fatigue

EIM Exercise in Medicine

HCP Health Care Provider

HEPA Health Enhancing Physical Activity

LPA Light Physical Activity

METs Metabolic equivalents of task

MPA Moderate Physical Activity

MOOC Massive Open Online Course

PA Physical Activity

PIM Practical Intervention Methodology

PUGS Public Urban Green Spaces

VPA Vigorous intensity Physical Activity

WHO World Health Organization





2. Glossary

Aerobic physical activity – Activity in which the body's large muscles move in a rhythmic manner for a sustained period of time. Improves cardiorespiratory fitness (Bull et al, 2020)

Balance – an individual's ability to control their centre of gravity within the limits of base of support (Sturnieks, 2021)

Balance training - static and dynamic exercises that are designed to improve an individual's ability to withstand challenges from postural sway or destabilizing stimuli caused by self-motion, the environment, or other objects (Bull et al, 2020)

Bone-strengthening activity – physical activity primarily designed to increase the strength of specific sites in bones that make up the skeletal system. Produce an impact or tension on the bones that promotes bone growth and strength (Bull et al, 2020)

Cancer Prevention Physical Activity – physical activity that may play a role in cancer prevention

Cancer Related Fatigue - is defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and that significantly interferes with usual functioning (Bower et al, 2014)

Exercise – a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective (Caspersen et al, 1985)





Light-intensity physical activity – on an absolute scale, refers to physical activity that is performed between 1.5 and 3 METs. On a scale of relative to an individual's personal capacity, usually a 2-4 on a rating scale of perceived exertion scale of 0-10 (Bull et al, 2020)

Moderate intensity physical activity – on an absolute scale refers to the physical activity that is performed between and 3 and <6 times the intensity of rest (METs). On a scale relative to an individual's personal capacity. On a scale of relative to an individual's personal capacity, usually a 5 o6 6 on a rating scale of perceived exertion scale of 0-10 (Bull et al, 2020)

Major muscle groups – include the legs, back, abdomen, chest, shoulders and arms (US Department of Health and Human Services, 2008)

Muscle-strengthening activity – Increase muscle strength, power, endurance and mass (Garber et al, 2011)

Physical activity – any bodily movement produced by skeletal muscles that requires energy expenditure (Caspersen CJ et al, 1985)

Physical inactivity – an insufficient physical activity level to meet present physical activity recommendations (Bull et al, 2020)

Physical exercise – A subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective. Physical activity includes exercise as well as other activities which involve bodily movement and are done as part of playing, working, active transportation, house chores and recreational activities (WHO, 2019)





Practical Intervention Methodology – contains guidelines and recommendations for physiotherapists and other health professionals for implementation of CPPA sessions for adults and senior citizens within PUGS in accordance with emerging scientific research evidence on cancer prevention (UcanACT — ERASMUS-SPORT-2021-SCP)

Prevention – Activities that are directed toward achieving and restoring optimal functioning, minimising impairments, limitations, and participation restrictions, maintaining health (thereby preventing further deterioration or future illness), creating appropriate environmental adaptations to enhance independent function.

- Primary prevention actions to avoid or remove the cause of a health problem in an individual or a population before it arises.
- Secondary prevention actions to detect a health problem at an early stage in an individual or a population, facilitating cure, or reducing or preventing spread, or reducing or preventing its long-term effects.
- Tertiary prevention actions to reduce the impact of an already established disease by restoring function and reducing disease-related complications (WHO, 2011; APTA, 2001)

Public Urban Green Space – land covered by vegetation of any kind, that is an important part of urban public open spaces and common services provided by an urban area (cities and towns) serving as a health-promoting setting for all members of the urban community (e.g., garden, parks, playground, urban meadow, urban woodlands, forests and natural wildlife areas) (WHO, 2017)

Sedentary behaviour – any waking behaviour characterized by an energy expenditure of 1.5 METS or lower while sitting, reclining, or lying (Bull et al, 2020)

Types of physical activity: occupational, recreational, domestic, active transport (Caspersen CJ, Powell KE. Christensen GM, 1985)





Vigorous-intensity physical activity – physical activity that is performed at 6.0 or more METs. On a scale relative to an individual's personal capacity, usually a 7 or 8 on a rating scale of perceived exertions scale of 0–10 (Bull et al, 2020)





3. Introduction to UcanACT

The project UcanACT project - Urban ACTion for cancer prevention: adult and senior citizens practice physical activity within public urban green spaces to prevent cancer diseases - is an intersectoral initiative funded by the European Union, and joining together physiotherapists, local authorities, non-profit organisations, higher education, and research institutions from eight organisations from five EU countries. Coordinated by the Europe Region of World Physiotherapy, the UcanACT partnership all come together to engage adult and senior citizens to practice physical activity (PA) as a tool for cancer prevention within public urban green spaces (PUGS).

The project addresses Erasmus Plus Programme Horizontal Priority "encouraging the participation in sports and physical activity" and its specific priority in the field of Sport, "the promotion of sport and physical activity as a tool for health". The project is also in line with EU Sport and Health Enhancing Physical Activity (HEPA) by promoting PA as a tool for cancer prevention.

The field of cancer prevention was chosen by the project partners due to the high urgency and importance of this topic for European public health. Cancer prevention, treatment and care are recognised by the von der Leyen Commission as a main priority in the area of health (Europe Beating Cancer Plan, 2021). The President of the European Commission stated that "unless we take decisive action, lives lost to cancer in the EU are set to increase by more than 24% by 2035, making it the leading cause of death in the EU."

In the EU 3.5 million people are diagnosed with cancer and 1.3 million die from it each year (Eurostat, 2018). The World Health Organisation (WHO), recognises cancer as a leading cause of death globally, with an estimated 10 million deaths from cancer in 2020, or nearly one in six deaths (WHO, 2022). The Robert Kock





institution and the Society for epidemiology cancer register in Germany report that everyone has a 50% risk of developing cancer (Centre for Cancer Registry). Around one third of deaths from cancer are due to tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake and lack of physical activity (WHO, 2022). Obesity is responsible for 6% of breast cancer, 8% of colon cancer and 34% or corpus uteri cancer, and as obesity rates increase because of physical inactivity and unhealthy diets, so will rates of these cancers (WHO IARC World Cancer Report, 2020).

Prevention of cancer is one of the most significant public health challenges of the 21st century (IARC,2011). Regular physical activity and maintaining a healthy body weight, after tobacco control, is the second most important means of cancer prevention. It is suggested that public health action is aimed at tackling these risk factors and physical activity should be encouraged (IARC, 2011).

Statistics data and research presented in the World Cancer Report (World Cancer Report WHO, 2020) indicate that between 30% and 50% of cancer deaths could be prevented by two ways:

- Modifying or avoiding key risk factors (among them: exercise regularly and maintaining health weight); and
- 2) Implementing evidence-based prevention strategies (one of them is practicing Health Enhancing Physical Activity (HEPA).

A possible measure for cancer prevention recognised by WHO is PA, which has been recognised scientifically on a global scale. 'Be physically active' is one of the Cancer Prevention Recommendations developed by the World Cancer Research Fund. Moreover, practicing physical exercise within open environments increases the positive benefits of PA (World Cancer Report, 2020). It is wiser to prevent a disease than to face its consequences at a more advanced stage.

Prevention is seen in the European Health policies as the touchstone of a redesigned system focused on improving health outcomes. Prevention advocates





have emphasised that it will save money, arguing that prevention is not only good for health but also a means to control spending. Economic value and cost effectiveness of cancer prevention is an important aspect that should be considered.

In sum, the UcanACT project aims at encouraging the participation of EU citizens in PA within PUGS and seeks to apply PA as a tool for cancer prevention for adults and senior citizens.





4. Desk Research Objectives

There is a lack of practical guidelines for physiotherapists and other health care professionals to provide cancer-prevention PA sessions, despite a growing number of scientific research proving that PA is a tool for cancer prevention and rehabilitation (World Cancer Report, WHO 2020). There is increasing evidence which shows that practicing PA within open nature environments increases the positive effects of cancer prevention, however existing recommendations on how to provide PA for cancer prevention are mainly done under clinical conditions (hospitals, rehabilitation centres) (Thompson Coon et al, 2011). PA within natural environments provides opportunities for social inclusion of cancer survivors and has a positive influence on mental health and lifestyle (Siqueira et al, 2007).

The project requires recent accurate scientific research demonstrating the positive benefits of PA for cancer prevention with a special focus on outdoor PA sessions. Special attention has been given to longitudinal research and research based on physiotherapy practice with cancer-prevention objectives.

The objectives of the desk research are aimed at discovering key characteristics of the Cancer Prevention Physical Activity (CPPA) that will be taken into consideration for building the Practical Intervention Methodology (PIM) and include:

- Cancer types that have scientifically approved classifications of reduced risk by practicing PA;
- Specificity of PA exercises for primary, secondary and tertiary prevention: dose and type of exercise;
- Safety and possible risk factors during the practice of CPPA.





The deliverable of this desk research (2.1) is a study with conclusions on positive benefits of PA for cancer prevention and recommendations for PIM development (D2.1).

The information and knowledge obtained and published in D2.1 will be used to develop new Practical Intervention Methodology (D3.1) that will be used for the Pilot Implementation (WP4).





5. Benefits of Physical Activity

Physical activity, across the full age spectrum, provides a variety of benefits. Some benefits happen immediately; a single episode of moderate-to-vigorous physical activity can improve sleep, reduce symptoms of anxiety, reduce blood pressure, and improve insulin sensitivity on the day the activity is performed. When physical activity is performed regularly, benefits and improvements become larger (PAGAC, 2018).

There is strong evidence to indicate that physical inactivity increases the risk of many adverse health conditions, including coronary heart disease, type 2 diabetes, and breast and colon cancer. This presents a major public health issue as much of the world's population is inactive (Lee et al, 2012).

In a study be Lee et al (2012) it was estimated that physical inactivity causes:

- 6% (3.2 -7.8%) of the burden of disease from coronary heart disease
- 7% (3.9 13.8%) of the burden of disease of colon cancer
- 9% (5.1 12.5) of premature mortality

If inactivity was decreased by 10% more than 533 000 deaths could be averted every year, and if inactivity was decreased by 25% more than 1.3 million deaths could be averted every year (Lee et al, 2012).

"Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it." — Plato (427–347 BC).





5.1. Benefits of Physical Activity in Older Adults

In older adults, higher amounts of sedentary behaviour are associated with poor health outcomes, while physical activity confers benefits for the following health outcomes (WHO, 2020):

- Improved all-cause mortality
- Cardiovascular disease mortality
- Incident hypertension
- Incident site-specific cancers
- Incident type-2 diabetes
- Mental health (reduced symptoms of anxiety and depression)
- Cognitive health

Physical activity helps prevent declines in bone health, functional ability and helps prevent falls and falls-related injuries (WHO, 2020).

WHO guidelines on physical activity and sedentary behaviour – older adults (2020)

Recommendations	Benefits	Evidence*
Older adults should do at least: - 150-300 minutes of moderate- intensity aerobic physical activity; or - 75-150 minutes of vigorous intensity aerobic physical activity; or - An equivalent combination of moderate and vigorous-intensity activity throughout the week	Substantial health benefits	Strong recommendation, moderate certainty evidence
Older adults should also do: - Muscle strengthening activities at moderate or greater intensity that involves all major muscle groups on 2 or more days a week	Provide additional health benefits	Strong recommendation, moderate certainty evidence





Older adults should do: - Varied multicomponent physical activity, that emphasises functional balance and strength training on 3 or more days a week	Enhance functional capacity Prevent falls	Strong recommendation, moderate certainty evidence
Older adults may: Increase moderate intensity aerobic physical activity to more than 300 minutes; or Do more than 150 minutes of vigorous-intensity aerobic physical activity; or an Equivalent combination of moderate and vigorous intensity activity throughout the week	For additional health benefits	Conditional recommendation, moderate certainty evidence
Older adults should: - Limit the amount of time spent sedentary; and - Replace sedentary-behaviour with physical activity of any intensity	Health benefits	Strong recommendation, moderate certainty evidence
Older adults should: - Aim to do more than the recommended levels of moderate to vigorous intensity physical activity	Reduce detrimental effects of high levels of sedentary behaviour	Strong recommendation, moderate certainty evidence

^{*} Strong - Balance of benefits to harm assessed as substantial for the target population for the recommendation.

5.2 Benefits of Physical Activity for Older Adults with Chronic Conditions

Regular physical activity is important in preventing and managing chronic conditions in older adults (PAGAC, 2018).



^{*} Conditional - Balance of benefits to harm assessed as small or important likely variability in benefits in the target population



WHO guidelines on physical activity and sedentary behaviour – adults and older adults with chronic conditions (2020)

older adults with chronic conditions (202		Evidence*
Recommendations	Benefits	Evidence*
Adults and older adults with these chronic conditions should do at least: - 150-300 minutes of moderate-intensity aerobic physical activity; or	Substantial health benefits	Strong recommendation, moderate certainty evidence
 75-150 minutes of vigorous intensity aerobic physical activity; or An equivalent combination of moderate and vigorous-intensity activity throughout the week 		
Adults and older adults with these chronic conditions should also do: - Muscle strengthening activities at	Provide additional health	Strong recommendation, moderate certainty
moderate or greater intensity that involves all major muscle groups on 2 or more days a week	benefits	evidence
Older adults with these chronic conditions should do: - Varied multicomponent physical activity that emphasises functional balance and strength training at moderate or greater intensity on 3 or more days a week	Enhance functional capacity Prevent falls	Strong recommendation, moderate certainty evidence
When not contraindicated, adults and older adults with these chronic conditions, may: - Increase moderate intensity aerobic physical activity to more than 300 minutes; or - Do more than 150 minutes of vigorous-intensity aerobic physical activity; or - An equivalent combination of	Additional health benefits	Conditional recommendation, moderate certainty evidence
moderate and vigorous intensity activity throughout the week for additional health benefits.		





Adults and older adults living with chronic conditions should: - Limit the amount of time spent being sedentary - Replace sedentary time with physical activity of any intensity	Provides health benefits	Strong recommendation, low certainty evidence
Adults and older adults with chronic conditions should: - Aim to do more than the recommended levels of moderate to vigorous-intensity physical activity	Reduce the detrimental effects of high sedentary behaviour on health	Strong recommendation, low certainty evidence

^{*} Strong - Balance of benefits to harm assessed as substantial for the target population for the recommendation.

5.3 Benefits of Physical Activity for Specific Conditions

Physical activity can confer health benefits for adults and older adults living with the following chronic conditions.

All-cause mortality (McKinney et al, 2016)

- Studies consistently demonstrate an inverse relationship between physical activity and rates for all-cause mortality

Cancer incidence and survival (WHO, 2020)

- Physical activity improves all-cause mortality, cancer-specific mortality, and risk of cancer recurrence or second primary cancer
- Physical activity promotes beneficial short- and long-term changes in metabolic, hormonal and inflammatory pathways
- Higher levels of physical activity after cancer diagnosis are reported to be protective for all-cause mortality following breast cancer, colorectal cancer, female reproductive cancer, glioma, kidney cancer, lung cancer, prostate cancer and stomach cancer
- Greater amounts of physical activity after cancer diagnosis are associated with lower risk of cause-specific mortality in breast cancer, colorectal cancer and prostate cancer survivors



^{*} Conditional - Balance of benefits to harm assessed as small or important likely variability in benefits in the target population



Primary prevention and management of hypertension (WHO, 2020)

- Physical activity improves physical function, cardiovascular disease progression and cardiovascular disease mortality
- Physical activity improves physical function
- Physical activity can improve health-related quality of life

Type-2 Diabetes (WHO, 2020)

- Physical activity reduces rates of mortality and indicators of disease progression
- Physical activity is associated with improved secondary indicators of risk progression (HnA1c, blood pressure, BMI and lipids)

HIV (WHO, 2020)

- Physical activity improves cardiorespiratory fitness
- Physical activity intervention can improve markers of cardiometabolic risk (lipids)
- Physical activity is positively associated with health-related quality of life and a reduction in symptoms of depression and anxiety
- Physical activity is associated with mean increase in lean body mass and decrease in percent body fate
- Physical activity does not adversely influence markers of HIV disease progression (CD4 count, or viral load)

Dementia (Livingston et al, 2020)

- Sustained exercise in midlife, and possibly later life, protects from dementia, possibly through decreasing obesity, diabetes, and cardiovascular risk
- Midlife systolic blood pressure control should aim for 130 mm Hg or lower to delay or prevent dementia

Osteoporosis (Benedetti et al, 2018)

- Physical activity stimulates bone osteogenesis in osteoporotic patients
- Walking alone does not appear to improve bone mass, however it is able to limit its progressive loss
- Progressive resistance training for the lower limbs appears to be most effective on BMD for the neck of the femur (post-menopausal women)
- Multicomponent training appears to be the most effective intervention for BMD at the spine (post-menopausal women)
- Weight bearing exercise with vibrating platforms may have an impact on BMD (post-menopausal women)

Frailty (Angulo J et al. 2020





- Frailty follows the combination of several impaired physiological mechanisms affecting multiple organs and systems
- Physical activity reduces age-related oxidation damage and inflammation and improved mitochondrial function
- Physical activity is considered a beneficial strategy to counteract physical impairment from frailty in the elderly.





6. Benefits of Physical Activity in Prevention of Cancer

Increased physical activity is an effective primary care cancer prevention, and it is recommended to implement community-wide public education and awareness campaigns for physical activity (WHO World Cancer Report 2020).

PA lowers the risk of seven types of cancers (bladder, breast, colon, endometrium, kidney, oesophageal adenocarcinoma and stomach cancer). There is moderate evidence for lower lung cancer risk (Physical activity guidelines advisory committee scientific report, 2018). Obesity is associated with increased risk of developing as many as 13 types of cancer, therefore physical activity can be used as a measure to mediate these risks (Kerr J, Anderson C, Lippman SM. 201 Physical activity, sedentary behaviour, diet and cancer: an update and emerging new evidence). Substantial reduction in tumour growth in response to PA has been demonstrated in preclinical studies with some studies citing reductions ranging between 31% and 67% (Roundtable report 2019). There are plausible biological mechanisms that may explain the benefits of PA in cancer prevention and control (Roundtable report on physical activity, sedentary behaviour and cancer prevention and control, American College of Sports Medicine).

It is known that the current WHO recommendation of physical activity can result in an overall 7% reduction, which is mainly to its protective role against breast cancer and colorectal cancer. Furthermore, the two-fold American College of Sports Medicine recommendation for a better health is considered to be the point of saturated protection against cancer (Liu et al., 2015).





6.1 Physical activity for primary cancer prevention

This section aims to summarize the existing evidence about the role of physical activity in the prevention of cancer in adult people. First, a comprehensive exposition of the effectiveness of physical activity in the prevention of different types of cancer is exposed; next, general physical activity recommendations as a modifiable risk factor for cancer prevention are disclosed. For these purposes, an exhaustic search of the most updated scientific findings has been conducted and a narrative description of this evidence is exposed below by cancer locations.

6.1.1 Bladder cancer

Most studies suggest that PA is a factor in the prevention of bladder cancer in healthy subjects. Active people involved in recreational or occupational activities have showed a reduction in the risk of bladder cancer from 15-40% (Rodríguez-Cintas et al., 2021; Keimling et al., 2014). Moreover, a linear association between physical activity dose and bladder cancer risk has been reported. Thus, the 25th, 50th, and 75th physical activity level percentiles were associated with reductions in bladder cancer risk of 10%, 14% and 17% respectively, with no differences between moderate to vigorous intensity (Keimling et al., 2014). A potential association of obesity with increased bladder cancer risk has been also observed (Noguchi et al., 2015). No statistically significant differences between genders were observed regarding the risk of developing bladder cancer (Keimling et al., 2014).

Keypoints:

- Recommended dose of moderate intensity PA can lead to a risk reduction of bladder cancer near to 15%.
- The highest the dose, the highest the risk reduction.
- Vigorous intensity does not have a stronger protective role.





6.1.2 Breast cancer

PA from moderate to vigorous intensity seems to decrease the risk of breast cancer (BC) in general (Gonçalves et al 2014, Hardefeldt et al. 2017, Namiranian et al. 2014, Neil-Sztramko et al. 2017, Pizot et al. 2016, Poorolajal et al. 2021). This relation is clear and most pronounced in postmenopausal women but evidence is not clear about premenopausal women or menopausal hormonal therapy treatment intake (Gonçalves et al. 2014, Neil-Sztramko et al. 2017, Pizot et al. 2016).

Significant dose-response relationship has been observed between amounts of physical activity and breast cancer risk indicating steady reductions in risk with increasing physical activity, without evidence for a threshold (Pizot et al. 2016, Poorolajal et al. 2021). For example, Namiranian et al. (2014) observed that physical activity less than 5,5 hour per week imply BC risk.

About risk population groups, findings suggest an interaction between PA and BMI. PA reduces BC risk on normal and overweight population (25<BMI<30) in similar amount but not in obese women (BMI >30) (Hardefeldt et al. 2017, Neil-Sztramko et al. 2017). Relation between PA and risk of BC is not clear regarding family history of BC or know breast cancer gene (BCRA1, BCRA2) (Hardefeldt et al. 2017).

Sedentary behavior within the occupational domain was associated with a 15.5% increased risk of breast cancer (Lee et al. 2021).

Keypoints:

- PA from moderate to vigorous intensity seems to decrease the risk of breast cancer (BC) in general.
- This relation is clear and most pronounced in postmenopausal women.





6.1.3 Colorectal cancer

There is a growing recognition on how PA is soundly associated with a reduced risk of colorectal cancer in conjunction with other lifestyle factors (e.g., diet, tobacco or alcohol) that may contribute to the aetiology of this type of cancer. It is known that an increased sedentary time (≥10h vs. 5h/day) is associated with an enhanced risk of early early-onset colorectal cancer (before 50 years old). This association seems to be mediated particularly by obesity, which is a well-known risk factor for several diseases, including colorectal cancer. Modifications in the gut microbiota species is likely to explain this relation (Puzzono et al., 2021). This protective role of PA has also been observed among people with a first-degree family history of colorectal cancer, which highlight the importance of PA as a health promotion strategy also in these high-risk subgroups (Shaw et al., 2018).

Keypoints:

- Having a physically active lifestyle in conjunction with other factors as healthy diet is crucial to reduce the risk of colorectal cancer.
- This reduction has been demonstrated even when a family history of this disease exists.

6.1.4 Endometrial cancer

Evidence supports a 20% reduction in risk of endometrial cancer when high versus low levels of physical activity are compared. The role of physical activity on endometrial cancer is significant for recreational activity, occupational activity, and walking/ biking for transportation, which includes activities of light, moderate and vigorous intensities. This protective factor is particularly strong for postmenopausal women who are overweight or obese (Schmid et al., 2015).

Keypoints:

- Even physical activity of light to moderate intensity, such as walking/biking for transportation, showed an apparent beneficial effect on this type of cancer risk.





6.1.5 Gastric cancer

A huge epidemiological analysis involving 15, 745 cases found that high versus low physical activity was associated with a gastroesophageal cancer risk decrease of 18%. Furthermore, the greatest risk reduction of 33 % was achieved by engaging in moderate to vigorous activity at a frequency of five times per week. A reduction in oxidative stress, chronic inflammation and metabolic disorders are some biological mechanisms that may mediate the observed inverse association between physical activity and gastroesophageal cancer (Behrens et al., 2014). A similar overall risk reduction of gastric cancer has been corroborated for any type of physical activity (total or recreational or occupational) (Psaltopoulou et al., 2016). Particularly to stomach cancer, physically active versus sedentary people are 0.83 times less likely to develop stomach cancer (Poorolajal et al., 2014).

Keypoints:

 Any type of moderate to vigorous activity at a frequency of five times per week seems to be the best dose for gastroesophageal cancer risk prevention.

6.1.6 Prostate cancer

Evidence about the protective effect of PA on prostate cancer is scarce. Findings suggested that there is not an association between leisure time PA, regardless of the intensity, and prostate cancer (Liu et al., 2018).

6.1.7 Testicular cancer

The evidence about the relationship between PA and testicular cancer is inconclusive. While some studies have observed a protective effect of PA another did not observe this relation (Huang et al., 2018).

Keypoints:

- Evidence about the protective effect of PA on prostate and testicular cancer is scarce and inconclusive.





6.1.8 Kidney cancer

Promising preliminary results supporting the protective factor of PA in kidney cancer risk have been reported. A risk reduction ranging from 34-12% has been observed when compared highest level of exercise (total or leisure occupational) to low. Moreover, kidney cancer seems to be associated to sitting time of more than nine hours/day (Al-Bayati et al. 2018; Behrens et al., 2013). Running or walking are activities that may reduce kidney cancer risk independently of the co-occurrence with other factor risks. It has been observed an incidence reduction of kidney cancer of 61% by running or walking by meeting the guidelines recommendations (7.5 to 12.5 MET-hours/week), 66.7% by running or walking 1-to 2-times the recommended levels and 76.2% by running or walking ≥2-times the recommended levels (Williams et al., 2014).

Keypoints:

- Even minimal recommended levels of exercise per week have demonstrated a protective role for kidney cancer prevention.

6.2. Physical activity for secondary and tertiary cancer prevention

6.2.1. Physical activity for secondary cancer prevention

According to the definition of Prevention, including in the Glossary, secondary prevention is defined as actions to detect a health problem at an early stage in an individual or a population, facilitating cure, or reducing or preventing spread, or reducing or preventing its long-term effects (WHO, 2011; APTA, 2001) (See Glossary section).

Although the benefits of physical activity in cancer patients have been demonstrated throughout the entire cancer patient pathway and in the prevention of its appearance (Europe Region, World Physiotherapy, 2022), in the case of





secondary prevention there are few studies focused on it, due to the above definition, since physical activity will not be used to detect either this health problem or the adverse effects that may arise from it and its treatments. On the other hand, it has a relevant role in their approach and treatment, as shown in the following section and corresponding to tertiary prevention (WHO, 2011; APTA, 2001).

6.2.2. Physical activity for tertiary cancer prevention

This section will be divided in two different stages of the patient's cancer pathway: physical activity during cancer treatment to prevent side effects and physical activity after cancer treatment and survivors for monitoring and treatment of long side-effects.

6.2.2.1. During cancer treatment

Pharmacological interventions for cancer: side effects of chemotherapy and radiotherapy

Chemotherapy is a commonly used therapy for advanced cancer, when the management of symptoms, quality of life and survival are prioritized. Higher doses and longer exposures of neurotoxic chemotherapy are associated with te greater risk and severity of chemotherapy-induced peripheral neuropathy (CIPN) (Crichton et al., 2021). In the most recent clinical practice guidelines no recommendations have been made for preventing CIPN, but certain pharmacological options, such as duloxetine, the only drug which has been widely supported by scientific evidence. Others (gabapentin, tricyclic antidepressants, opioids or lidocaine), despite the scarcity of evidence, are beginning to be used to manage symptoms. In addition to the limited efficacy, these drugs lead to numerous side effects, like nausea, dizziness and drowsiness. Due to the occurrence of these side effects, non-pharmacological





interventions are emerging as an alternative to drugs to cope with the consequences of chemotherapy.

Non-pharmacological therapies: Physical activity for tertiary prevention during cancer treatment

Bruinsma et al (2021) proved in a meta-analysis that exercise interventions and combined exercise and diet interventions had little effect on circulating inflammatory mediators. However, exercise had a significant effect on leptin levels in breast cancer survivors suggesting that leptin may be a possible mediator of exercise—induced changes in breast cancer recurrence.

There is strong evidence for the role of exercise prescription to manage the following side effects: anxiety, depressive symptoms, fatigue, health related quality of life, lymphoedema and physical function. There is moderate evidence for the role of exercise in the management of bone health and sleep in patients living with cancer (Campbell et al., 2019).

Not only can physical activity reduce those symptoms, but the combination of exercising with other healthy lifestyle habits may also help reduce cancer mortality risk (Molina et al., 2021).

Fatigue

Fatigue is one of the most frequent and distressing side effects of cancer treatment. This symptom affects up to 70% of patients during chemotherapy and radiotherapy (Arnold et Taylor, 2010). Low resistance exercise undertaken at a moderate-to-high intensity is sufficient to achieve significant fatigue and quality of life benefits for men with prostate cancer, and also mitigate depression and anxiety symptoms. A lower resistance exercise dosage than usually prescribed may help enhance adherence by reducing exercise barriers (López et al., 2021). According to Chen et al. who conducted a meta-analysis to determine the effectiveness of exercise in advanced-stage cancer, exercise (either resistance





or aerobic exercise, or combined) may be an effective intervention to counter fatigue as well as anxiety, and depressive symptoms (Chen et al., 2019).

Nevertheless, some other authors consider that evidences still need to be more solid to confirm the benefits of aerobic exercise training for fatigue during and after cancer therapy, mainly when there are solid tumours, and suggest future research needs to focus on determining the optimal type, intensity and timing of an exercise intervention (Cramp et al., 2012; Kangas et al., 2008).

Keypoints:

 In advanced-stage cancer, exercise (either resistance or aerobic exercise, or combined) may be an effective intervention to counter fatigue.

Neuropathic pain

Chemotherapy-induced peripheral neuropathy is present in approximately 30-90% patients who have undergone neurotoxic chemotherapy (Guo et al., 2022). Exercise may be beneficial for improving neuropathic pain by counteracting the effects of chemotherapy on the nervous central system (Crichton et al., 2022), and it is a safe, cost-effective and ideal adjuvant intervention to chemotherapy, although there is no strong evidence to support any recommendations about the need to exercise to prevent and deal with neuropathic pain.

Keypoints:

- Exercise may be beneficial for improving neuropathic pain, and it is a safe, cost-effective and ideal adjuvant intervention to chemotherapy.

Weakness

Cancer therapeutical interventions my cause weakness as an important adverse side effect (Jones et al., 2011). Resistance exercises have been shown to be





effective in the improvement of physical function, increasing muscle strength and muscle mass (Keilani et al. 2017), in men with prostate cancer (Bourke et al., 2015).

The review performed by Cavalheri et al. (2019) showed that fitness level and legs strength were better compared to those who didn't exercise, and the research conducted by Cheema et al. (2020) indicates that resistance training was beneficial for physical functioning, increasing strength and suggest that clinical practice guidelines should be updated to inform health care providers on the benefits.

These are only a few examples of studies which have demonstrated the effectiveness of physical activity in the improvement of muscle strength.

Keypoints:

- Resistance training is beneficial for physical functioning, increasing strength.
- Clinical practice guidelines should be updated to inform health care providers.

Reduced range of movement

Cancer may be associated with inflammation, which can lead to fatigue and reduction of the range of movement (Dennet et al., 2016). Some exercise interventions were delivered during cancer chemotherapy or radiation therapy, whereas others were delivered following cancer treatment, which resulted in better outcomes concerning physical function. Statistical differences have been found between center-based supervised exercise and home-based unsupervised exercise for the variables mood, physical function and quality of life, whose outcomes are better when exercise was supervised (Conn et al., 2006).

Four studies assessed the shoulder range of movement in women with breast cancer by means of goniometry (Pinto-Carral et al., 2018), and an important improvement was found after a Pilates programme, although the authors believe





there wouldn't be differences between Pilates and any other type of physical activity intervention.

Keypoints:

- Exercise interventions resulted in better outcomes concerning physical function.
- Mood, physical function and quality of life improvement is far better when exercise was supervised.

Lymphedema

Approximately 20% of breast cancer patients develop lymphedema within the first 2 years after diagnosis. Its severity may progress over time from mild edema to severe, chronic edema, and is associated with pain, heaviness, and tightness in the affected region (Hayes et al., 2022). Exercise was found to be effective in the prevention of lymphedema occurrence, regardless of the type of exercise (aerobic, resistance, or both).

Keypoints:

- Exercise may be effective in the prevention of lymphedema occurrence, regardless the type of exercise.

Cardiopulmonary function

Cancer surgery, potentially followed by chemotherapy, radiotherapy, immunotherapy and/or hormone therapy may result in muscular weakness, increased body mass and declines in cardiorespiratory fitness (Boing et al., 2020).

Aerobic exercise during or after cancer adjuvant therapy seems to be an effective effect on cardiopulmonary function and decreases the percentage of body fat in women with breast cancer (Kim et al., 2009). Exercise during radiation therapy in





prostate cancer patients has also been associated with a better physical function, among other benefits (Schumacher et al., 2021).

Supervised exercise training is associated with significant improvements in VO2 peak following a diagnosis of early-stage cancer, with minimal adverse effects (Jones et al., 2011).

Eight Randomized Conrolled Trials (RCTs), evaluated dyspnoea among 564 patients, with important results and improvement in comparison to the group of participants undergoing usual care (Chen et al., 2019).

Keypoints:

- Aerobic exercise during or after cancer adjuvant therapy seems to be an effective effect on cardiopulmonary function.
- Supervised exercise training is associated with significant improvements in VO2 peak following a diagnosis of early-stage cancer.

6.2.2.2. After treatment: survivors

Cancer survivors are almost three times more likely to report fair or poor health after cancer treatment and also, they are twice more likely to have psychosocial disabilities and physical and functional limitations in comparison with persons without cancer (Hewitt et al, 2003). The most common side effects of cancer disease and cancer treatment are fatigue, poor quality of life and emotional distress (Siegel et al, 2019), also some of the problems or adverse effects as a consequence of the treatments received, such as functional limitation, dyspnea and risk of recurrence and even death, can continue.

Fatigue

Cancer-related fatigue (CRF) has been highlighted by patients as the most disabling symptom during and after completion of treatment (Al-Mqbali et al, 2021).





There are many studies that have focused on showing the effectiveness of exercise or physical activity on this symptom in these patients, and some systematic reviews and meta-analyses showed these results (Cramp et al, 2012; Tomlison et al 2014; (Bourke et al, 2015) Whether they are studies focused on aerobic exercises (Juvet et al 2017), home physical activity (Huizinga et al 2021), or on a multimodal program, all have found that these programs are effective in improving fatigue.

However, some recommendations are specified for the application of these exercise programs in these patients, such as the preference of carrying out exercises supervised instead of home exercises without any supervision, in this case promoting not only the improvement of fatigue or quality of life but also adherence to exercise; On the other hand, in terms of intensity, moderate intensity exercise programs are recommended, which show greater effectiveness (Ferrer et al, 2010); Its application in the elderly shows greater effectiveness than in the young population; and when they are carried out together with providing education and guidance, they show better results (Huizinga et al, 2021, Brown et al, 2011).

For all these reasons, the authors recommend that after cancer treatment, the clinician might encourage more physical activity enhancing interventions in CRF. (Hilfiker et al, 2018).

Keypoints:

- Cancer related fatigue is also a disable symptom after treatment.
- Exercise or PA is effective after completion of treatment.
- Supervised exercise is more recommended that home exercise without supervision.
- Moderate intensity exercise programs with education and guidance show better effectiveness.





Depression

Depression is a symptom frequently associated with cancer patients or arises as a consequence of treatment (Massie, 2004). However, its appearance varies depending on the type of cancer, but it affects the quality of life of patients in a very negative way. (Somerset, 2004).

Given the impact it entails for cancer survivors, Craft et al, showed in 2012 that a supervised exercise program of at least 30 minutes had a positive effect on depressive symptoms (Craft et al, 2012). And later, Salam et al, found a significant improvement in depression levels when carrying out an exercise program, suggesting that these values would decrease even more if it started after the cancer diagnosis (Salam, 2022).

Keypoints:

- This symptom depends on the type of cancer but affect negatively to quality of life of patients.
- Supervised exercise programs of at least 30 minutes have a positive effect.
- These should start after cancer diagnosis to decrease these symptoms even more.

Functional impairment

Cancer survivors have less physical functionality, added to the effects of age (Brown et al, 2016), which place them in a fragile position compared to those who have not suffered from cancer (Bennet et 2013). This situation is also diminished in those cases in which comorbidities are present.

As an approach to this symptom, authors such as Swartz et al (2017), have shown physical activity carried out in the community as a potential tool to combat this functional deterioration in older cancer survivors. Data that correspond to those obtained by Keplin et al (2013), in terms of the beneficial effect, in this case





of an exercise program for this population, but they highlight the need to apply the program individually for reasons of safety, efficacy and to optimize motivation.

Keypoints:

- Functional impairment added to age and other comorbidities is a challenge for cancer survivors.
- Exercise programmes in the community and individually have a positive effect in these symptoms but individually programs are better for reason of safety, efficacy and motivation.

Risk of death and recurrence

Several studies have recently emerged that show the protective effect that physical activity and exercise have both on cancer recurrence and on mortality in cancer survivors (Morishita et al, 2020; Molina-Montes et al, 2021).

Although most of them focus on breast cancer, Zagalaz-Anula et al (2022), show how cancer-associated mortality can be reduced by 37% in post-diagnosis physical activity, data that increases to 39% when moderate exercise is performed routinely on a daily basis, showing these authors physical activity as a protector in this type of cancer. (Salam et al, 2022)

In the same line and for the same type of cancer, Miyamoto et al and Spei et al studies (Miyamoto et al 2022; Spei et al, 2013) obtained similar results, a 35% reduction in cancer recurrence and a favourable impact on cardiovascular mortality, respectively, but both were focused on recreational physical activity carried out in a more intense way, these results may enhance the motivation of cancer survivors.

Keypoints:

- Exercise and PA have a protective effect on recurrence and risk of death in patients.





Quality of life

Cancer survivors have many adverse effects of a physical and psychological nature as a result of cancer and the treatment received. As a result, they have a poorer quality of life than those who have not suffered from it, consequently affecting all areas of their lives. Improving this quality of life is an objective of treatment for cancer survivors, and where physical activity and exercise have shown to be effective as extracted from different systematic reviews and meta-analyses. Mishra et al (2012), shows that exercise not only improves the overall quality of life but also details the improvement in aspects such as the emotional sphere, anxiety, fatigue, social life, sexuality or pain in different follow-up periods. However, more research is needed in relation to the maintenance of these long-term effects, which should be associated with adherence to treatment and a change in lifestyle, where the data are still low (Smith SG, Chagpar AB, 2010). Promoting healthy lifestyles that include exercise or physical activity improves survival from cancer, as in bladder cancer among others studied, and health-related quality of life (Rodriguez-Cintas et al, 2021).

It is also necessary to deliver into the characteristics of exercise according to the type of cancer and treatment and its impact on quality of life and its different domains (Mishra et al, 2012).

Bourke et al (2016), state for prostate cancer that the treating clinician should play a role indirectly advocating the benefits of exercise to men with prostate cancer and leading the multidisciplinary team in the referral process, given the effectiveness shown in improving the quality of life of these men and to promote adherence to exercise and lifestyle changes (Bourke et al, 2015)

Keypoints:

- Exercise and PA have shown to have an effective impact in quality of life in cancer survivors.
- Adherence to treatment and changes in lifestyle could increase the maintenance of long-term effects on quality of life.





While exercise guidelines and research are in place for cancer patients during and after treatment, physiotherapists have an important role in the prescription of individualised exercise programmes to engage patients in an active life and to enable to meet these guidelines. (Europe Region of World Physiotherapy, 2022)





7. Risk factors and barriers for physical activity in cancer prevention

Historically, clinicians advised cancer patients to rest and to avoid activity; however, emerging research on exercise has challenged this recommendation. The advice to "avoid inactivity," even in cancer patients with existing disease or undergoing difficult treatments, is likely helpful. Physical Activity (PA) is safe before, during and after cancer treatments and results in improvements in preventing cancer and improving physical functioning, quality of life, and cancer-related fatigue in several cancer survivor groups. In the last two decades, it has become clear that exercise plays a vital role in cancer prevention and control. Recently, the American College of Sports Medicine has updated its exercise guidance for cancer prevention as well as for the prevention and treatment of a variety of cancer health-related outcomes (e.g., fatigue, anxiety, depression, function, and quality of life). The expert panel affirm that there is sufficient evidence to support the efficacy of specific doses of exercise training to address cancer-related health outcomes, including fatigue, quality of life, physical function, anxiety, and depressive symptoms (Campbell, Kristin L et al., 2019).

A summary of this evidence is provided in the following table:

LEVEL OF EVIDENCE Benefits of exercise in cancer patients			
STRONG	MODERATE	INSUFFICIENT	
Anxiety reduction	Sleep	Cardiotoxicity	
Fewer depressive symptoms	Bone health (Not for metastases)	Chemotherapy-induced peripheral neuropathy	
Reduce fatigue		Cognitive functions	
Better Quality of Life (Qol)		Falls	





Perceived phisical function improvement	Nausea
No risk for upper extremity lymphedema exacerbation	Pain
	Sexual function
	Treatment tolerance

Despite these guidelines, the majority of people living with and beyond cancer are not regularly physically active. Reports indicate that 60-70% of people with cancer do not meet aerobic exercise guidelines and it is estimated that 80-90% do not meet resistance exercise guidelines (Eakin, Elizabeth G et al, 2007). Among the reasons for this is a lack of clarity on the part of those who work in oncology clinical settings of their role in assessing, advising, and referring patients to exercise (Schmitz, Kathryn H et al., 2019). To do this will require care coordination with appropriate professionals as well as change in the behaviors of clinicians, patients, and those who deliver the rehabilitation and exercise programming. Behavior change is one of many challenges to enacting the proposed practice changes. Other implementation challenges include capacity for triage and referral, the need for a program registry, costs and compensation, and workforce development.

In conclusion, there is a call to action for key stakeholders to create the infrastructure and cultural adaptations needed so that all people living with and beyond cancer can be as active as is possible for them. Despite the numerous benefits of physical activity (PA) for patients with cancer, many cancer survivors report challenges to participating in PA. The barriers could be a lot and depending on patients, on environment and other internal or external factors. Romero, Sally A D et al., 2018 in a survey involving 662 patients found the following evidences, putting Fatigue and Pain on the top list of barriers:





Barriers	Endorsing %
Busy/No Time	29.1
Low Motivation	67.2
Low Discipline	65.2
Lack of safe environment	10.5
Lack of financial resources	20.1
Nausea	35
Fatigue	77.6
Pain	71
Sadness	31.8
Treatment side effects	50.7
Surgical complications	21.2
Doctor saying not to exercise	6.4

Multiple studies of breast, colorectal, prostate, and a mixed cohort of cancer survivors noted that greater than 80% of patients were interested in receiving advice from their oncology care team. Despite this, studies suggest that 9% of nurses and from 19% to 23% of oncology physicians refer patients with cancer to exercise programming. A recent survey of 971 oncology clinicians that was conducted by the American Society of Clinical Oncology indicated that 78.9% of respondents agreed that oncology clinicians should recommend physical activity to their patients. Observed barriers to clinicians referring patients to exercise programming include lack of awareness of the potential value of exercise in cancer populations, uncertainty regarding the safety or suitability of exercise for a particular patient, lack of awareness regarding available programs to help facilitate exercise in cancer populations, need for education and skills development for making referrals, and a belief that referrals to exercise programming are not within the scope of practice for oncology clinicians. In





summary, the scientific evidence base supports exercise, and patients and clinicians generally agree that patients should be moving throughout their cancer therapy and survivorship. Translating from the current state to exercise assessment, advice, referral, and engagement as standard practice for all people living with and beyond cancer is a multifactorial puzzle to be solved. The Excercise is Medicine (EIM) initiative was launched by the ACSM in 2007 with the goal of incorporating physical activity assessment, advice, and referral as a standard part of patient health care for the prevention and treatment of chronic diseases. The EIM approach arose in part from successful clinical trials that trained primary health care providers (HCPs) to refer patients to exercise programming. To date, the EIM approach has been adopted in several primary health care clinics, the evidence base strongly supports adoption of the EIM approach for all patients with chronic conditions, including people living with and beyond cancer. Patients need referral to appropriate exercise programming based on their current activity levels, medical status, and preferences. Some patients may already be regular exercisers and/or may prefer to exercise on their own, however current evidence indicates that exercise under supervision yields better outcomes. Especially during treatment, patients are at risk for developing side effects that are a barrier to exercise. Patients may underestimate how the treatment might affect their ability to exercise on their own.





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