

### STUDY ON ECONOMIC VALUE AND COST EFFECTIVENESS OF PHYSICAL ACTIVITY CANCER- PREVENTIVE MEASURES

DELIVERABLE 4.6 CONTRIBUTION TO WP4 – IMPLEMENTATION AND EVALUATION OF PILOT PROGRAMME

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- Foundation of the Europe Region of World Physiotherapy (ERWP)

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#### **Abbreviations**

CEA: Cost-effectiveness analysis CUA: Cost-utility analysis **CRF:** Cancer-Related Fatigue questionnaire DASH: Disabilities of the Arm, Shoulder, and Hand EORTC: European Organisation for Research and Treatment of Cancer EORTC-QLQ-BR23: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Breast Cancer Function and Symptoms scales EORTC-CR29: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Colorectal Cancer module EORTC-QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire EORTC-QLQ-PR25: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Prostate Cancer EQ-5D: European Quality of Life-5 Dimensions FAACT-B+4-MS: Functional Assessment of Cancer Therapy-Breast ICERs: Incremental cost-effectiveness ratios NNT: Number Needed to Treat PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses QALYs: Incremental quality-adjusted life-years RCTs: Randomised controlled trials **RR:** Relative risk SF-12: 12-Item Short-Form Health Survey SF-36: 36-Item Short-Form Health Survey WTP: willingness-to-pay WHO: World Health Organization



#### Summary

**Introduction.** Scientific evidence supports the effectiveness of exercise and physical activity in the prevention and treatment of various types of cancer, as well as in improving patient survival and quality of life. However, although there are indications that exercise interventions may be cost-effective, the evidence remains limited. Therefore, the purpose of this report was to systematically review current evidence on the cost-effectiveness of exercise therapy in cancer population.

**Methods.** A systematic review of economic evaluations performed alongside randomised controlled trials (RCTs) was developed. An electronic search was conducted in five databases and study selection and data extraction was independently performed by two reviewers. Differences in costs and incremental cost-effectiveness ratios (ICERs) were descriptively analysed.

**Results.** A total of 653 records were identified from the databases, of which 10 reports (9 RCTs) recruiting 2,344 participants (mean age 56.2 years, 87% female) were finally included. Breast cancer was the most commonly studied cancer, followed by colorectal cancer and prostate cancer.

**Conclusions.** Evidence suggests that the cost-effectiveness of exercise therapy in cancer population may be variable, depending on factors such as the type of cancer, the timing of the intervention and the extent of the costs considered. The heterogeneity observed in the different economic studies makes it difficult to draw general conclusions and to directly compare the findings reported in different studies. Future economic evaluations on this topic should be desirable, as they can provide valuable insights and inform policy decisions.



#### **1. Introduction**

Physical activity is known to benefit a range of health outcomes in adults, improving all-cause mortality, mental and cognitive health and sleep, symptoms of anxiety and depression, and obesity (WHO, 2020). Specifically in cancer prevention, we know that between 30% and 50% of cancer deaths could be prevented by modifying or avoiding key risk factors and implementing existing evidence-based prevention strategies (WHO, 2020).

There is strong epidemiological evidence that being physically active reduces the risk of several types of cancer, including bladder (Rodríguez-Cintas et al., 2021, Keimling et al., 2014), breast (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), colon (Puzzono et al., 2021; Shaw et al., 2018), endometrium (Schmid et al., 2015), kidney (Al-Bayati et al., 2018; Behrens et al., 2013; Williams et al., 2014), oesophagus and stomach (Behrens et al., 2014; Psaltopoulou et al., 2016; Poorolajal et al., 2020).

In contrast, higher levels of physical inactivity are associated with poor health outcomes in older adults (WHO, 2020), and sedentary behaviour is known to be associated with an increased risk of different types of cancer (Wild et al., 2020; National Cancer Institute, 2020). A recent umbrella review comprising 77 original studies concluded that high sedentary behaviour levels increase the relative risk (RR) for developing ovarian (RR: 1.29), endometrial (RR: 1.29), colon (RR: 1.25), breast (RR: 1.08), prostate (RR: 1.08), and rectal cancers (RR: 1.07). In addition, the same study also reported an increased risk of cancer mortality of 1.18 (95% CI = 1.09-1.26) (Hermelink et al., 2022).

Beyond cancer prevention, there is strong evidence of the role of physical activity to manage some cancer side effects, such as anxiety, depressive symptoms, fatigue, health related quality of life, lymphoedema and physical function (Campbell et al., 2019; Gupta et al., 2025). In addition, several studies have highlighted the protective effect of physical activity and exercise on both cancer recurrence and mortality in cancer survivors (McTiernan et al., 2019; Bui et al.,



2025; Cormie et al.; 2017, Dong et al., 2025; Gunnell et al., 2017; Perrier et al., 2025).

## Cost-Effectiveness and Cost-Utility of Exercise in Cancer Prevention and Treatment

The concepts of cost-effectiveness and cost-utility are essential for evaluating the economic feasibility of exercise interventions in the oncology setting. Cost-effectiveness assesses the cost of an intervention in relation to its clinical effectiveness, whereas cost-utility incorporates quality-adjusted life years (QALYs) as an outcome measure.

A systematic review of cost-effectiveness studies on physical activity interventions in cancer survivors from high-income countries found that some interventions were cost-effective; however, the results varied depending on the intensity of the activity and the clinical context (Gubler-Gut et al. 2021).

As we have seen, scientific evidence supports the effectiveness of exercise and physical activity in the prevention and treatment of various types of cancer, as well as in improving patient survival and quality of life. However, although there are indications that exercise interventions may be cost-effective, the evidence remains limited, and further research is needed to accurately determine the cost-benefit of these interventions across different cancer types.

Therefore, the purpose of this report was to systematically review current evidence on the cost-effectiveness of exercise therapy in cancer population.



#### 2. Methods

To provide the most robust synthesis of the evidence on the cost-effectiveness of exercise-based interventions in the cancer population, this report has been developed in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Page et al., 2020).

#### 2.1 Data sources and search strategy

The search was conducted in PubMed, Embase, PsycInfo, CINHAL and SPORTDiscus databases from their inception to November 2024. Among others, Medical Subjects Heading (MeSH) terms as "exercise", "training" or cancer were used, adapting the search strategy to the different databases requirements. The full search strategy for each database is reported in **Table 1**.



#### Table 1. Search strategies.

| PUBMED      | (("cost analy*"[Title/Abstract] OR "cost benefit*"[Title/Abstract] OR "cost<br>utilit*"[Title/Abstract] OR "cost-minimization"[Title/Abstract] OR "cost-<br>effectiveness"[Title/Abstract] OR "cost-effective"[Title/Abstract] OR "cost<br>efficien*"[Title/Abstract] OR "economic evaluation"[Title/Abstract] OR "conomic<br>analy*"[Title/Abstract] OR "health-economic"[Title/Abstract] OR "value of<br>money"[Title/Abstract]) AND ("exercise"[Title/Abstract] OR "physical<br>activity"[Title/Abstract] OR "training"[Title/Abstract]) AND ("cancer"[Title/Abstract] OR<br>"oncology"[Title/Abstract] OR "palliative"[Title/Abstract] OR "metasta*"[Title/Abstract]))<br>AND ((randomizedcontrolledtrial[Filter]) AND (humans[Filter]))   |
|-------------|--|
| EMBASE      | ('cost analy*':ti,ab,kw OR 'cost benefit*':ti,ab,kw OR 'cost utilit*':ti,ab,kw OR 'cost minimization':ti,ab,kw OR 'cost effectiveness':ti,ab,kw OR 'cost effective':ti,ab,kw OR 'cost effectiv |
| CINHAL      | AB (cost analy* OR cost benefit* OR cost utilit* OR cost minimization OR cost effectiveness OR cost effective OR cost efficien* OR economic evaluation OR economic analy* OR health economic OR value for money) AND AB (exercise OR physical activity OR training) AND AB (cancer OR oncology OR palliative OR metasta*) AND AB random*   |
| SPORTDISCUS | AB (cost analy* OR cost benefit* OR cost utilit* OR cost minimization OR cost effectiveness OR cost effective OR cost efficien* OR economic evaluation OR economic analy* OR health economic OR value for money) AND AB (exercise OR physical activity OR training) AND AB (cancer OR oncology OR palliative OR metasta*) AND AB random*   |
| PSYCINFO    | abstract(cost analy* OR cost benefit* OR cost utilit* OR cost minimization OR cost<br>effectiveness OR cost effective OR cost efficien* OR economic evaluation OR economic<br>analy* OR health economic OR value for money) AND abstract(exercise OR physical<br>activity OR training) AND abstract(cancer OR oncology OR palliative OR metasta*) AND<br>abstract(random*)   |



#### 2.2 Eligibility criteria

We defined our eligibility criteria **(Table 2)** following the accepted PICOS framework for literature search (P: Population, I: Intervention, C: Comparison, O: Outcomes, S: Study Design) as follows (Eriksen & Frandsen, 2018):

Inclusion criteria:

**(P):** People over 18 years old with any type of cancer diagnosis (stages I-IV). They can be undergoing primary adjuvant treatments (e.g. chemotherapy or radiation therapy) or have finalized them (survivorship phase) (Khan et al., 2012).

(I): Any type of physical exercise (e.g., endurance/aerobic, resistance/strengthening, stretching, coordination) as defined by the World Health Organization (WHO): 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 (Bull et al., 2020).

For inclusion, a clear exercise prescription based on duration, frequency, and/or intensity had to be set. Moreover, physical exercise should be applied as a single intervention.

(C): Any intervention other than physical exercise or absence of intervention.

(O): Costs and/or incremental cost-effectiveness ratios (ICERs).

**(S):** Economic evaluations performed alongside randomised controlled trials (RCTs) that conducted a cost analysis, cost-effectiveness and/or cost-utility analysis.

The exclusion criteria were: RCTs involving prehabilitation exercises or multimodal interventions that combine exercise programs with other non-exercise



interventions. RCTs based on general exercise recommendations were also excluded. There were no language or publication date restrictions.

| Inclusion criteria   | Exclusion criteria  |
|--|---|
| Randomised controlled trials including:  | Randomised controlled trials including:   |
| <ul> <li>Adults with a diagnosis of any<br/>type of cancer in treatment or<br/>survivors</li> </ul>                            | <ul> <li>Prehabilitation exercises or<br/>multimodal interventions<br/>(exercise plus another therapy)</li> </ul> |
| <ul> <li>Any type of physical exercise<br/>intervention as defined by the<br/>WHO and apply as a single<br/>therapy</li> </ul> | General exercise     recommendations without clear     prescription parameters                                    |
| <ul> <li>Any intervention other than<br/>exercise or no intervention as<br/>comparator</li> </ul>                              |   |
| <ul> <li>Costs and/or incremental cost-<br/>effectiveness ratios (ICERs) as<br/>economic evaluation outcomes</li> </ul>        |   |

#### 2.3 Study selection

Two reviewers independently performed the study selection process. They first removed duplicates using Mendeley desktop citation management software (v1.19.8) and screened titles and abstracts of all records using the PICOS eligibility criteria mentioned above. The full texts were then assessed. Disagreements between reviewers were resolved by discussion (6 studies) and, if necessary, a third reviewer was consulted (2 studies).



#### 2.4 Data extraction and data synthesis

Data were extracted from each study by two independent reviewers. A customised data extraction sheet was used to collect the following data: bibliometric data (ie, first author, year of publication, country, related RCT), characteristics of participants (i.e., cancer site, under treatment/survivor, sample size by groups and mean age), intervention details (i.e., exercise modality, duration, frequency, intensity), type of control group, health outcomes and points of assessment), economic evaluation (i.e., type of analysis, outcome indicator, time horizon and analysis perspective) and main findings. This information was synthesised and displayed in tables of studies characteristics. Finally, costs and incremental cost ratios were synthesised descriptively.

#### 3. Results

#### 3.1 Study selection

A total of 653 records from databases were identified of which 24 were full-text retrieved. Finally, 10 reports (9 RCTs) were included (**Figure 1**). **Table S1** contains a full list of the records excluded in the last step (n= 14) and reasons.

The two studies by Gordon et al. (2017 and 2020) originate from the same clinical trial (Hayes et al., 2013). Therefore, they are considered as a single study in the clinical synthesis (n=9), but are considered separately in the economic synthesis (n=10) as they focus on different time horizons.





Figure 1. PRISMA 2020 flow diagram.



#### 3.2 Participants' characteristics description

In the nine selected randomised clinical trials, a total of 2,344 participants were included (n = 1,382 in the experimental group and n = 962 in the control group). Concerning sample characteristics, the mean age was 56.2 years, and 87% were women (n = 2,036), most of whom were diagnosed with breast cancer (n = 1,978), although 22 had colorectal cancer and 40 had multiple myeloma. Among the male participants (n = 308), 2 had breast cancer, 202 had prostate cancer, 55 had colorectal cancer, and 67 had multiple myeloma or lymphoma.

#### 3.3 Exercise interventions and comparators description

Most of the analysed studies implemented interventions combining aerobic exercise (e.g., walking, running, or cycling) with resistance training. Exceptions include Mewes et al. (2015), which applied aerobic training only, and Ax et al. (2022), which included two experimental groups - one receiving both aerobic and resistance training, and the other receiving aerobic training alone.

The duration of the interventions varied, ranging from 12 weeks (Mewes et al., 2015) to 9 months (Schoute et al., 2025). Ax et al. (2022) was the only study to conduct an 18-month follow-up, while both Haines et al. (2010) and Bruce et al. (2021) included a 12-month follow-up.

Although programme structures varied across studies, most included sessions of approximately 60 minutes. Depending on session frequency, the total weekly training volume ranged from 120 minutes (Edmunds et al., 2020; Schoute et al., 2025; van Dongen et al., 2019), to 150 minutes (Ax et al., 2022; Mewes et al., 2015), and up to 180 minutes per week in Gordon et al. (2017, 2020) and May et al. (2017). Regarding supervision, only a subset of these studies incorporated professional oversight (Ax et al., 2022; Bruce et al., 2021; Edmunds et al., 2020; May et al., 2017; Schoute et al., 2025; van Dongen et al., 2025; van Dongen et al., 2017).



In terms of training intensity, volume, dosage, and progression, there was considerable variability across studies. For instance, Ax et al. (2022) compared two experimental groups: one underwent progressive resistance training increasing from 6 to 10 RM, while the other trained only up to 50% of 10 RM. Similarly, Edmunds et al. (2020) implemented resistance training with 2 to 4 sets of 12 repetitions at 6 RM, while aerobic training targeted 70–85% of maximum heart rate, corresponding to 11–13 points on the Borg Rating of Perceived Exertion Scale (6–20 scale).

In contrast, Gordon et al. (2017, 2020) adjusted exercise progression based on individual participant capacity, as did Schoute et al. (2025), May et al. (2017), Mewes et al. (2015), and van Dongen et al. (2019). Other studies, such as Bruce et al. (2021) and Schoute et al. (2025), reported greater exercise intensity among participants who adhered to the intervention compared to those in the control group.

# 3.4 Results of the exercise interventions on clinical outcomes: effectiveness

Although this review focuses on the economic impact of exercise therapy for cancer, it also presents a synthesis of the clinical results of the primary RCTs on which the economic evaluations are based. The focus on clinical variables required a search for the original clinical trials that included all measured variables. These are larger clinical trials such as Phys-Can (Demmelmaier et al, 2021), the PACT study (Travier N et al., 2015), the EFFECT study (Hiensch AE et al., 2024), the EfH trial (Hayes et al., 2013) or the EXIST study (Persoon S et al., 2017), which were consulted to obtain the results and clinical effectiveness of the intervention in patients with various types of cancer (**Table 3**).



Primary RCT Economic report Ax et al., 2022 Demmelmaier et al., 2021. PhysCan Project Edmunds et al., 2020 Galvão et al., 2014. RADAR trial Gordon et al., 2017, 2020 Haves et al., 2013. EfH trial Travier et al., 2015. PACT trial May et al., 2017 Van Vulpen et al., 2016 PACT trial Mewes et al., 2015 Duijts et al., 2012 Hiensch et al., 2022. PREFERABLE EFFECT Schouten et al., 2025 trial van Dongen et al., 2019 Persoon et al., 2017. EXIST trial

**Table 3.** Original RCTs from which clinical data have been extracted.

#### 3.4.1. Quality of Life

The variable consistently assessed across all the analysed studies was quality of life. Later, in the cost-effectiveness analysis, we will examine the usefulness of this measure in determining to what extent the cost of the intervention translates into improvements in quality of life. However, data were also obtained regarding the clinical effectiveness of the intervention in the experimental groups in terms of quality of life.

Of the nine studies included in this analysis, eight utilised quality of life scales such as the SF-36, EORTC, or EQ-5D-3L, with the exception of the study by Gordon et al. (2017,2020), which employed the FACT-B-4 scale.

The results following the experimental interventions were heterogeneous; however, most studies (Bruce et al., 2021; Edmunds et al., 2020; Gordon et al., 2017; Gordon et al., 2020; Haines et al., 2010; Mewes et al., 2015; Schouten et al., 2025) reported improvements in patients' quality of life. Only the studies by Ax et al. (2022) and van Dongen et al. (2019) did not demonstrate a measurable improvement in this outcome (**Table 4**).



#### 3.4.2. Fatigue

In the six studies that measured this variable (Ax et al., 2022; Gordon et al., 2017; Gordon et al., 2020; Haines et al., 2010; May et al., 2015; Schouten et al., 2025; van Dongen et al., 2019), we found a predominant use of the Cancer Related Fatigue questionnaire (CRF) for data collection (Ax et al., 2020; Haines et al., 2010; May et al., 2015; van Dongen et al., 2019). Other studies used the Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F) scale (Gordon et al., 2017), the eFACIT-F questionnaire, the Fatigue Quality List (May et al., 2015), and the EORTC Cancer-related Fatigue QLQ-FA12 (Schouten et al., 2025).

Data on cancer-related fatigue show differing results across studies. Four of them show significantly lower levels of physical fatigue in the intervention group compared to the control group, with the Ax et al. (2022) study highlighting improvements favoring the high-intensity exercise group compared to the low-moderate-intensity group. In contrast, Haines et al. (2015) and van Dongen et al. (2019) respective studies found no significant differences in fatigue levels between the comparison groups (**Table 4**).

#### 3.4.3. Lymphoedema

The occurrence of limb oedema was analysed in two of the studies included in this review (Bruce et al., 2021; Haines et al., 2010). Circumferential measurements or simple clinical observation were used as assessment tools. Any study found significant differences between baseline measurements and those taken after the intervention (**Table 4**).



#### 3.4.4. Upper limb functionality

Of the nine studies included, only two collected data on participants' upper limb function (Bruce et al., 2017; Gordon et al., 2017,2020). Both used the same measurement instrument: the DASH questionnaire.

The results of the two studies are completely opposite. While Bruce et al. (2017) obtained statistically and clinically significant data in favour of the intervention group, the study by Gordon et al. (2017, 2020) did not obtain significant differences between the study groups (**Table 4**).

#### 3.4.5. Physical Function: Physical/cardiorespiratory capacity

General physical and cardiorespiratory capacity was assessed in four studies using various measurement tools. These included the modified Balke protocol (Ax et al., 2022), the 3-minute step test (Gordon et al., 2017; Gordon et al., 2020), the 6-minute walk test (Haines et al., 2010), and the 400-meter walk test along with the chair rise test (Edmunds et al., 2020). Only the study by Edmunds et al. (2020) reported significant differences between baseline and post-intervention measurements in the tests employed (**Table 4**).

#### 3.4.6. Pain: postoperative and neuropathic

Of the studies included in this review, only four collected data on pain, either as postoperative pain (Bruce et al., 2021), as neuropathic pain (Bruce et al., 2021; Gordon et al., 2017; Gordon et al., 2020), or as a dimension of quality of life (May et al., 2017; Schouten et al., 2024).

Regarding postoperative pain, Bruce's study showed that pain intensity improved at 12 months in the intervention group compared to usual care.



Regarding neuropathic pain, both Bruce et al. (2021), and Gordon et al. (2017,2020) showed no differences between the groups. The data collected on pain as a dimension of quality of life, using the EORTC-QLQ-C30 questionnaire, are inconsistent between the two studies. On the one hand, the primary studies of May et al. (2017) showed a negative effect size for pain, compared to Schouten et al. (2025), who presented beneficial and clinically relevant results for pain. Finally, the study by Haines et al. (2010) does not include pain as one of its outcome variables, although it does report the onset of pain as an adverse effect of exercise. Musculoskeletal pain occurred in 9 subjects in the sample, three in the control group and six in the intervention group. Of these, three reported the onset of pain while performing their programmes, two in the intervention group

and one in the control group, which forced them to discontinue the activity (**Table 4**).

#### 3.4.7. Body composition

The studies by Edmunds et al. (2020), Gordon et al. (2017,2020), and Haines et al. (2010) examined the effectiveness of the intervention in modifying body composition. Bioelectrical impedance analysis was used in the studies by Gordon et al. (2017, 2020) and Haines et al. (2010), while dual-energy X-ray absorptiometry (DEXA) was employed in the study by Edmunds et al. (2020). Notably, only the Edmunds et al. (2020) study reported a significant improvement in body composition at six months post-intervention (**Table 4**).



#### Keypoints on clinical outcomes measures:

- Although the experimental interventions varied across the studies included, the majority reported improvements in patients' quality of life.
- Higher-intensity exercise was associated with reduced levels of physical fatigue.
- Postoperative pain intensity showed improvement at 12 months in the intervention groups compared to usual care. However, evidence supporting the effectiveness of exercise on neuropathic pain remains insufficient, despite some beneficial and clinically meaningful outcomes being reported.
- There is not enough evidence supporting the effectiveness of the intervention in improving upper limb function, lymphoedema, body composition or general physical and cardiorespiratory capacity, although several studies showed significant differences.



#### **Table 4**. Description of the studies included based on primary RCTs.

| Author(s), year<br>Country<br><i>Related RCT</i> | Cancer site, sample<br>size (mean age, SD)<br><i>Under</i><br>treatment/survivor | Type of<br>exercise<br>training and<br>control<br>condition | Clinical outcomes<br>Assessment points | Main findings on<br>clinical outcomes | Main conclusions<br>on clinical<br>outcomes |
|--|--|---|--|---------------------------------------|---|
|  | Breast, colorectal,  | High-intensity  | » Cancer-related                       | There were small but                  | Patients                                    |
|  | and prostate cancer  | (HI) and low-to-  |  | significant between-                  | undergoing (neo)                            |
|  | (N=619)  | moderate (LIVII)  | » Quality of life (QoL)                | group differences in                  | adjuvant treatment                          |
|  | $\Gamma O(n - \Gamma O A)$ , means   |   | » Mood                                 | physical fatigue,                     | for breast, prostate                        |
|  | EG ( $n = 534$ ): mean   | resistance and  |  | muscle strength and                   |   |
| Ax et al., 2022                                  | age 59 $(\pm 10)$  | endurance   | » Cardiorespiratory                    | fitness in feveral II                 |   |
|  | CG (n = 85): mean  | exercise  |  | nuness in layour or Hi                | exercise at HI or                           |
| Sweden   |  | programme   |  | exercise.                             | their own                                   |
|  | ondergoing (neo)   | Control groups HI   | TO. Daselline, TT. O                   |                                       | nell Own                                    |
| Phys-Can trial                                   | trootmont  |   | monuns                                 |                                       | Additional BCS                              |
|  | liealment  |   |  |                                       | Auditional BCS                              |
|  |  |   |  |                                       | avtra bonofit in                            |
|  |  | BCS, LIVII PIUS   |  |                                       |   |
|  |  |   |  |                                       | controlled evercise                         |
|  |  |   |  |                                       | interventions                               |
|  |  | l   |  |                                       |   |

| 0    |  |   |   |   |   |  |  |
|------|--|---|---|---|---|--|--|
| Ucai | Bruce et al.,<br>2021<br>United<br>Kingdom<br>PROSPER trial            | Breast cancer women<br>with high risk of upper<br>limb disability after<br>surgery (n= 382)<br>EG (n= 191): mean<br>age 58.4 (± 12.2)<br>CG (n= 191): mean<br>age 57.8 (± 12)<br>Undergoing adjuvant<br>oncological treatment | Resistance,<br>endurance and<br>mobility exercise<br>programme<br>Control group:<br>usual care (no<br>further<br>intervention<br>other than<br>leaflets provided<br>during<br>preoperative                                      | <ul> <li>» Upper limb function</li> <li>» Postoperative pain</li> <li>» Arm symptoms</li> <li>» Wound related</li> <li>complications</li> <li>» Lymphoedema</li> <li>» Quality of life</li> <li>T0: baseline; T1: 6</li> <li>weeks; T2: 6 months;</li> <li>T3: 12 months</li> </ul> | The exercise<br>programme improved<br>upper limb function,<br>postoperative pain,<br>arm symptoms, and<br>physical quality of life<br>at 12 months,<br>compared with the<br>control condition.  | An early,<br>structured,<br>progressive<br>exercise is sa<br>and clinically<br>effective for<br>women at hig<br>of developing<br>shoulder and<br>upper limb<br>problems after<br>non-reconstru-<br>breast surger | afe<br>gh risk<br>g<br>er<br>uctive<br>ry.                               |
| _    | Edmunds et<br>al., 2020<br>Australia and<br>New Zealand<br>RADAR trial | Long-term prostate<br>cancer survivors (n=<br>100)<br>EG (n= 20): mean age<br>71.9 (± 5.6)<br>CG (n= 50) mean<br>age:71.5 (± 7.2)<br>Survivor phase   | clinics)<br>Resistance and<br>endurance<br>exercise<br>programme<br>Control group:<br>usual care with a<br>general<br>recommendation<br>to perform 150 of<br>moderate<br>physical exercise<br>per week with<br>printed material | <ul> <li>» Cardiorespiratory<br/>fitness</li> <li>» Lower-body<br/>functional performance</li> <li>» Muscle strength</li> <li>» Quality of life</li> <li>» Body composition</li> <li>» Biomarkers</li> <li><i>T0: baseline; T1: 6</i><br/>months; <i>T2: 12 months</i></li> </ul>   | The exercise<br>programme improved<br>cardiorespiratory<br>fitness, lower-body<br>function, muscle<br>strength, self-<br>reported physical<br>functioning and<br>appendicular skeletal<br>muscle, compared<br>with the control<br>condition ( $T_1$ ).<br>Most benefits were<br>maintained in the<br>long-term ( $T_2$ ). | Supervised<br>exercise train<br>long-term pro-<br>cancer surviv<br>more effectiv<br>physical activ<br>educational<br>material for<br>improving a k<br>range of physical<br>health outcor                         | ning in<br>ostate<br>vors is<br>e than<br>vity<br>proad<br>sical<br>mes. |
|      | Gordon et al.,<br>2017   | Breast cancer women<br>after surgery (n= 194)   | Resistance and endurance  | » Quality of life   | There were significant between-   | Exercise can<br>considered a   | be<br>s a  |

| $\bigcirc$                   |   |  |  |   |   |   |
|------------------------------|---|--|--|---|---|---|
| Jcar<br>hysical Activity for | Gordon et al.,<br>2020<br>Australia<br><i>EfH trial</i> | EG1 (n= 67): mean<br>age 51.2 (± 8.8)<br>EG2 (n= 67): mean<br>age 52.2 (± 8.6)<br>CG (n= 60): mean<br>age 53.9 (± 7.7)<br>Undergoing adjuvant<br>oncological treatment         | exercise<br>programme<br>delivered face-<br>to-face (EG1) or<br>by telephone<br>(EG2)<br>Control group:<br>no intervention,<br>only information<br>related to<br>exercises<br>following breast<br>cancer | <ul> <li>» Treatment-related<br/>symptoms: fatigue,<br/>menopausal<br/>symptoms, neuropathic<br/>pain and<br/>lymphoedema</li> <li>» Cardiorespiratory<br/>fitness</li> <li>» Muscle strength<br/><i>T0: baseline; T1: 6</i><br/><i>weeks; T2: 6 months;</i><br/><i>T3: 12 months</i></li> </ul>  | group differences in<br>QoL, fitness and<br>fatigue in favour of<br>both EG.<br>Trends observed for<br>the treatment groups<br>were similar.  | form of adjuvant<br>breast cancer<br>therapy that can<br>prevent declines in<br>fitness and<br>function during<br>treatment and<br>optimise recovery<br>post-treatment. |
|                              | Haines et al.,<br>2010<br>Australia                     | Breast cancer women<br>after surgery (n= 89)<br>EG (n= 46): mean age<br>55.9 (± 10.5)<br>CG (n= 47): mean<br>age 54.2 (± 11.5)<br>Undergoing adjuvant<br>oncological treatment | Resistance,<br>endurance and<br>balance exercise<br>programme<br>Control group:<br>sham flexibility<br>and relaxation<br>exercises   | <ul> <li>» Quality of life</li> <li>» Upper limb swelling</li> <li>» Body composition</li> <li>» Cancer-related</li> <li>fatigue</li> <li>» General physical</li> <li>capacity: endurance,</li> <li>strength, balance and</li> <li>shoulder range of</li> <li>motion (ROM)</li> <li>T0: baseline; T1: 3</li> <li>months; T2: 6 months;</li> <li>and T3:12 months</li> </ul> | There were<br>significant between-<br>group differences in<br>QoL, physical<br>function and upper<br>limb swelling at T1 in<br>favour of both EG.<br>These improvements<br>were not sustained<br>beyond this point. | Provision of<br>multimodal<br>exercise<br>programmes will<br>improve the short-<br>term health of<br>women undergoing<br>adjuvant therapy.                              |
|                              | May et al.,<br>2017                                     | Breast and colon<br>cancer (n= 194)  | Resistance and endurance   | » Cancer-related<br>fatigue<br>» Quality of life  | Breast cancer:<br>There were<br>significant between-  | Exercise early<br>during treatment of<br>breast and colon   |

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| Pryskal Active for Can PACT trials          | EG breast cancer (n=<br>87): mean age 50.0<br>(±7.9)<br>EG colon cancer (n=<br>14): mean age 57.4<br>(±11.2)<br>CG breast cancer (n=<br>78): mean age 49.4<br>(±7.6)<br>CG colon cancer (n=<br>15): mean age 59.1<br>(±8.9)<br>Undergoing adjuvant<br>oncological treatment | exercise<br>programme<br>To be physically<br>active for at least<br>30 min a day/3<br>days a week<br>Control group:<br>usual care.<br>Maintainance of<br>habitual physical<br>activity pattern | <ul> <li>» Cardiorespiratory<br/>fitness</li> <li>» Muscle strength</li> <li>» Body mass index</li> <li>» Physical activity level</li> <li><i>T0: baseline; T1: 18</i><br/>weeks; <i>T2: 36 weeks</i></li> </ul> | group differences in<br>physical fatigue (T1),<br>cardiorespiratory<br>fitness (T1) and<br>muscle strength (T1)<br>in favour of the EG.<br>Colon cancer:<br>There were<br>significant between-<br>group differences in<br>physical fatigue (T1<br>and T2) and quality<br>of life (T1 and T2) in<br>favour of the EG. | cancer can be<br>recommended.  |
| <i>Mewes et al.,</i><br>2015<br>Netherlands | Breast cancer (n=<br>213)<br>EG1 (n= 104): mean<br>age 47.7 (± 5.6)<br>EG2 (n=109): mean<br>age 48.2 (± 5.7)<br>CG (n= 103): mean<br>age 47.8 (± 6)<br>Survivor phase   | EG1: endurance<br>exercise<br>programme (60-<br>80% VO <sub>2max</sub> )<br>EG2: cognitive<br>behavioural<br>therapy (CBT)<br>CG: waiting list   | <ul> <li>» Endocrine symptoms</li> <li>» Perceived burden of<br/>hot flashes/night<br/>sweats</li> <li>» Quality of life<br/><i>T0: baseline; T1: 12</i><br/>weeks; <i>T2: 6 months</i><br/>follow-up</li> </ul> | There were<br>significant overall<br>effects favoring the<br>intervention groups<br>in all outcomes (T0<br>and T2)   | Physical exercise<br>and CBT can have<br>salutary effects on<br>endocrine<br>symptoms and, to<br>a lesser degree,<br>on sexuality and<br>physical<br>functioning of<br>patients with<br>breast cancer<br>experiencing<br>treatment-induced<br>menopause. |

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| Uca               | Schouten et   | Metastatic breast     | Resistance,         | » Physical fatigue   | Exercise resulted in   | Supervised             |
| Physical Activity | all., 2025    | cancer (n= $357$ )    | endurance and       | » Quality of life    | significant positive   | exercise nas           |
|                   | Nothorlands   | FG (n = 178); mean    | programme           | nonthe: T2: 6        | primary outcomes       | on physical fatique    |
|                   | Nethenanus    | age 54 9 (+11 6)      | programme           |                      | Physical fatique was   | and Ool in             |
|                   | PREFERABLE-   |                       | Control group:      |                      | significantly lower    | patients with          |
|                   | EFFECT        | CG (n=179): mean      | usual               |                      | QoL significantly      | ,<br>metastatic breast |
|                   | trial         | age 55.9 (±10.7)      | care,               |                      | higher in the exercise | cancer and should      |
|                   |               |                       | supplemented        |                      | group than in the      | be                     |
|                   |               | Undergoing adjuvant   | with general        |                      | control group at 6     | recommended as         |
|                   |               | oncological treatment | activity advice     |                      | months                 | part of supportive     |
|                   |               |                       | and an activity     |                      |                        | care.                  |
|                   |               |                       | liacker             |                      |                        |                        |
|                   |               |                       |                     |                      |                        |                        |
|                   |               |                       |                     |                      |                        |                        |
|                   | van Dongen et | Multiple myeloma or   | Resistance and      | » Cardiorespiratory  | No statistically       | The lack of            |
|                   | al., 2019     | lymphoma (n= 109)     | endurance           | fitness              | significant            | significant            |
|                   |               |                       | exercise            |                      | differences were       | intervention effects   |
|                   | Netherlands   | EG (n= 54): mean age  | programme           | » Handgrip strength  | found between the      | may relate to          |
|                   | EXIST trial   | 52 (±11)              |                     |                      | intervention and       | suboptimal timing      |
|                   |               | 00 (** 55) ****       | Control group:      | » Cancer-related     | control group at short | of intervention        |
|                   |               | CG (n=55): mean age   | usual care          | Tatigue              | and long-term.         | delivery,              |
|                   |               | 55 (±12)              | according to        | » Quality of life    |                        | the control group      |
|                   |               | Lindergoing adjuvant  | natients' and       |                      |                        | and/or subontimal      |
|                   |               | oncological treatment | physicians'         | T0: baseline: T1: 18 |                        | compliance to the      |
|                   |               |                       | preferences.        | weeks: T2: 12 months |                        | prescribed             |
|                   |               |                       | Control group       | -,                   |                        | exercise               |
|                   |               |                       | patients were not   |                      |                        | intervention.          |
|                   |               |                       | restricted in their |                      |                        |                        |

| physical<br>activities or ir<br>their use of<br>healthcare<br>services. | ו |  |
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#### Abbreviations:

**BCS:** behaviour change support; **CBT:** cognitive behavioural therapy; **CG:** control group; **EG:** experimental group; **EfH:** Exercise for Health; **HI:** high-intensity; **LMI**: low-to-moderate intensity; **ROM:** range of motion; **QoL**: quality of life.



#### 3.5 Economic analysis description

Nine of the ten economic evaluations performed a cost-effectiveness analysis and/or a cost-utility analysis. Only Ax et al. (2022) conducted a cost analysis (**Table 5**). The most common outcome measure used in cost-effectiveness assessments was Quality-Adjusted Life-Years (QALYs) (Bruce et al., 2021; Edmunds et al., 2020; Gordon et al., 2017; Gordon et al., 2020; Haines et al., 2010; May et al., 2017; Mewes et al., 2015; Schouten et al., 2025, van Dongen et al., 2019). In addition, Mewes et al. (2015) used measures of relevant symptom reduction (menopausal symptoms in breast cancer survivors) as the primary outcome for their cost-effectiveness analysis, rather than QALYs. They also calculated the Number Needed to Treat (NNT) to achieve this difference. Van Dongen et al. (2019) also included other clinical outcomes such as physical fitness (cardiorespiratory fitness, grip strength) and fatigue in their cost-effectiveness analyses, in addition to QALYs.

Regarding the perspective of the economic evaluation, five of the ten reports adopted a societal perspective in the economic analysis, which is the broadest and includes costs to the health system, the intervention and society (such as lost productivity) (Ax et al., 2022; Edmunds et al., 2020; Haines et al., 2010; May et al., 2017; van Dongen et al., 2019). Others used a health system perspective (Bruce et al., 2021; Edmunds et al., 2020), which focuses on costs to the health system. One included sensitivity analysis from a social perspective (Schouten et al. 2025) and two of the studies focused on a broad perspective covering healthcare providers, patients, and government (Gordon et al., 2017; Gordon et al., 2020). The time horizon is another determinant of the results of the economic analysis and in our case, it ranged from six months (Ax et al., 2022) to eight years (Gordon et al., 2020). A more detailed description of the economic analysis can be found in **Table 6.** 



**Table 5.** Description of economic methods.

#### Cost-effectiveness analysis (CEA)

- The results of the intervention are measured in natural units (life years gained or number of patients surviving) by the difference between the results obtained in the intervention group versus the control group.
- The main indicator for decision-making is the Incremental Cost-Effectiveness Ratio (ICER), which is calculated as the difference in total costs divided by the difference in the specific outcome measure between the intervention and the comparator.
- The results should be read as the additional cost that is necessary to achieve one more year of life or one more survivor.

#### Cost-utility analysis (CUA)

- The CUA is a specific type of CEA where the health outcome is measured in generic units that combine quantity and quality of life gained.
- The most common outcome measure is Quality-Adjusted Life-Years (QALYs), which are obtained from measures of health-related quality of life, such as those derived from cancer-specific questionnaires, the EQ-5D (EQ-5D-3L or EQ-5D-5L) or the SF-36.
- The ICER in a CUA is expressed as the additional cost that needs to be incurred to achieve an additional unit of QALY gained.
- The CUA is useful for comparing the cost-effectiveness of interventions targeting different health conditions, as QALYs provide a common metric.
- Outcomes are often benchmarked against willingness-to-pay (WTP) thresholds for a QALY. This benchmark is derived using statistical estimation procedures and is different for different countries and years.
- Intervention is considered 'dominant' if it is simultaneously less costly and more effective (generates more QALYs) than the comparator.

#### Costs analysis

- It quantifies and compares the costs and resources used by the intervention group versus the control group, without going into health outcomes.
- The analysis is done from a social perspective and includes those of exercise intervention, medical care and lost productivity.



#### **Table 6.** Summary of the characteristics of the economic analysis.

| Author(s), year<br>Country                              | Main<br>methodology<br>used                                   | Outcome indicator  | Analysis<br>perspective  | Relevant additional notes  |
|---|---|--|--|--|
| Ax et al., 2022<br>Sweden                               | Cost Analysis   | Resource use (outpatient visits,<br>hospitalisation days,<br>medications, sick days) and<br>total/disaggregated costs                            | Social, including<br>healthcare system<br>costs and<br>productivity losses         | Focused on quantifying and comparing<br>costs and resource use. Health outcome<br>metrics such as QALYs or cost per unit of<br>specific effect were not included. ANCOVA<br>analysis and t-tests were used for<br>comparisons. No discounting was applied                  |
| Bruce et al.,<br>2021<br>United<br>Kingdom              | Cost-Utility<br>Analysis (CUA)                                | Quality-Adjusted Life Years<br>(QALYs) (derived from the EQ-<br>5D-5L), Incremental cost per<br>QALY gained, Incremental Net<br>Monetary Benefit | NHS and Personal<br>Social Services  | Analysis within a randomised controlled trial<br>(RCT) with a 12-month time horizon. No<br>discounting was applied. Multiple imputation<br>was used for missing data. Cost-<br>effectiveness acceptability curves (CEACs)<br>were used.                                    |
| Edmunds et al.,<br>2020<br>Australia and<br>New Zealand | Cost-<br>Effectiveness<br>Analysis (CEA),<br>specifically CUA | QALYs (estimated from the SF-<br>36/SF-6D), Incremental cost per<br>QALY gained  | Healthcare-Payor<br>(baseline analysis)<br>and Social<br>(sensitivity<br>analysis) | Analysis within a trial with a 6-month time<br>horizon. No discounting was applied.<br>Maximum likelihood and multiple imputation<br>were used for missing QALYs. Cost-<br>effectiveness acceptability curves (CEACs)<br>and a cost-effectiveness plane were<br>presented. |
| Gordon et al.,<br>2017<br>Australia                     | Cost-<br>Effectiveness<br>Analysis,<br>including CUA          | QALYs (derived from the EQ-<br>5D-3L), Incremental cost per<br>"improver"  | Broad (covering<br>healthcare<br>providers, patients,<br>and government)           | Evaluated cost-effectiveness versus usual<br>care. Time horizon was 12 months. One-<br>way and probabilistic sensitivity analyses<br>were performed.   |

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| Jcar<br>Physical Activity for | Gordon et al.,<br>2020<br>Australia     | Cost-<br>Effectiveness<br>Analysis using a<br>Markov model  | QALYs, Life Years, Incremental<br>Cost-Effectiveness Ratio (ICER)  | Implicitly<br>broad/social (uses<br>varied data,<br>including mortality<br>and recurrence) | Cohort-based analysis of the remaining life<br>span. A 5% annual discount rate was<br>applied to costs, QALYs, and life years.<br>Adherence to CHEERS guidelines. Use of<br>one-way and probabilistic sensitivity<br>analyses.  |
|                               | Haines et al.,<br>2010<br>Australia     | Cost-Utility<br>Analysis (CUA)  | QALYs (derived from the utility<br>component of the EQ-5D),<br>Outcomes based on the VAS<br>component of the EQ-5D | Social   | Economic evaluation over a 6-month time<br>horizon. Cost-effectiveness acceptability<br>analysis was performed using bootstrap.<br>Linear mixed models were used to analyse<br>HQoL outcomes.   |
|                               | May et al., 2017<br>Netherlands         | Cost-<br>Effectiveness<br>Analysis,<br>specifically CUA   | Adjusted QALYs, Incremental<br>Cost-Effectiveness Ratio (ICER)   | Social   | Prospective economic evaluation in an<br>RCT. The time horizon is not explicitly<br>detailed in the abstract, but appears to<br>encompass the intervention (18 weeks) plus<br>follow-up. A "bottom-up" microcosting<br>method was used for intervention costs.<br>Use of cost-effectiveness acceptability<br>curves and planes. |
| -                             | Mewes et al.,<br>2015<br>Netherlands    | Cost-<br>Effectiveness<br>Analysis (CEA)<br>and Cost-Utility<br>Analysis (CUA)<br>using a Markov<br>model | Incremental cost per<br>"improvement" (on FACT-ES,<br>HFRS scales), Costs per QALY<br>gained                       | Dutch healthcare<br>system   | Analysis based on an RCT. Use of a 5-year<br>Markov model. Discounting was applied to<br>costs (4%) and effects (1.5%). One-way<br>and probabilistic sensitivity analyses were<br>performed. Use of cost-effectiveness<br>acceptability curves and planes.  |
|                               | Schouten et al.,<br>2025<br>Netherlands | Cost-Utility<br>Analysis (CUA)  | QALYs (derived from the EQ-<br>5D-5L), Incremental cost per<br>QALY gained   | Social (base case)<br>and Healthcare<br>(scenario)   | Analysis in a multinational RCT. 9-month<br>time horizon. Use of the bottom-up method<br>for intervention costs. Multiple imputation<br>was used for missing data. Bootstrapping,<br>cost-effectiveness planes, and acceptability<br>curves were used. "Dominant" interventions   |

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| Ucar<br>Physical Activity for | Cancer Prevention                         |  |   |        | (least expensive and most effective) were identified.  |
|                               | Van Dongen et<br>al., 2019<br>Netherlands | Cost-<br>Effectiveness<br>Analysis,<br>including CUA | Incremental cost per unit of<br>natural outcomes (e.g.,<br>cardiorespiratory fitness, grip<br>strength, fatigue), Costs per<br>QALY gained (derived from the<br>EQ-5D-3L) | Social | Long-term cost-effectiveness assessment<br>(1-year post-intervention). Microcosting was<br>used for intervention costs. Discounting was<br>applied to post-1-year costs (4%). Multiple<br>imputation was used for missing data.<br>Bootstrapping, cost-effectiveness planes, |
|                               |   |  | ,   |        | and acceptability curves were used.  |

#### Abbreviations:

**CEA:** cost-effectiveness analysis; **CHEERS:** Consolidated Health Economic Evaluation Reporting Standards; **CUA:** cost-utility analysis; **EQ-5D-3L:** Euroqol -five dimensions -three levels; **EQ-5D-5L:** Euroqol -five dimensions -five levels; **FACT-ES:** Functional Assessment of Cancer Therapy – Endocrine Symptoms; **HFRS:** Hospital Frailty Risk Score; **HQoL:** health realet quality of life; **ICER:** incremental cost utility ratio; **NHS:** National Health Service; **QALYs:** quality-adjusted life-years; **RCT:** randomised controlled trial; **SF-36:** short form health survey; SF-6D: short form-six dimensions health survey; **VAS:** visual analogue scale.



#### 3.6 Results of economic evaluations: cost-effectiveness

#### 3.6.1 Costs

Almost all studies reported the cost of the exercise intervention, detailing its components (professionals, facilities, materials). In general, direct results on whether exercise is more costly or saves money are inconsistent. Some studies suggest that exercise may be less costly or have similar costs to usual care (May et al., 2017-colon cancer; Schouten et al., 2025). In these cases, the cost of the intervention may be offset by savings in medical care or improvements in productivity. Other studies found that exercise was associated with similar total costs (Ax et al., 2022; Van Dongen et al., 2019), but with trade-offs between different types of costs (e.g. higher health care costs offset by lower productivity/informal care costs). Ax et al. (2022) also reported savings in disability pension costs in favour of exercise intervention. In contrast, May et al. (2017) found that exercise intervention was associated with higher costs in breast cancer, with no clear benefit to guality of life, while Edmunds et al. (2020) reported no evidence of cost savings in subsequent resource use (drugs, health services) or loss of productivity in prostate cancer survivors. Finally, Mewes et al. (2015) concluded that exercise had slightly higher incremental costs than usual care and higher than cognitive behaviour therapy (CBT) to achieve certain outcomes, although the total 5-year costs were similar to CBT (Table 7).

#### 3.6.2 Incremental cost-effectiveness ratios

The heterogeneity described in cost estimates, outcome measures, patient populations, study designs, intervention characteristics and health care systems make comparisons difficult. Therefore, in general, there was no clear trend in the cost-effectiveness results for exercise-based interventions in the cancer population.



• Cost-effective or dominant:

Four of the ten trials reported results in favour of exercise interventions. May et al. (2017) found that exercise was cost-effective and dominant (least costly and most effective) for patients with colorectal cancer, with a 100% probability of being cost-effective. Schouten et al. (2025) found that supervised exercise was dominant (more effective and at similar or lower cost) from a societal perspective for patients with metastatic breast cancer in both 1:1 and 1:4 supervised settings. The costs of the intervention were offset by health care and productivity savings, and the intervention was highly likely to be cost-effective (65%-91% at the willingness-to-pay threshold of  $\in$ 20,000/QALY). Similarly, Bruce et al. (2021) reported that the likelihood of the intervention being cost-effective increased significantly when the costs of other cancer treatments were removed. Finally, Haines et al. (2010) reported that the intervention had higher costs for medical care, but significantly lower costs for unpaid productivity and informal care (**Table 7**).

No cost-effective:

Four of the ten trials reported results that did not clearly support the costeffectiveness of exercise interventions. May et al. (2017) found that exercise was not cost-effective for breast cancer patients, as it was associated with higher costs without a clear effect on quality of life. The probability of being cost-effective was low (2% at  $\in$ 20,000/QALY). Similarly, Van Dongen et al. (2019) found a low probability of cost-effectiveness for exercise after stem cell transplantation, and the overall cost difference remained in favour of the control group in the main analysis. Finally, Gordon et al. (2017, 2020) showed different ICER results in their sensitivity analyses, including scenarios where 'usual care dominates' (**Table 7**).



#### **UcanACT Table 7.** Summary of the main economic findings.

| Author(s),<br>year<br>Country                           | Currency,<br>cost year | Main costs   | Summary of findings  | Time Horizon | Analysis<br>perspective                          | Keypoints  |
|---|------------------------|--|--|--------------|--|--|
| Ax et al.,<br>2022<br>Sweden                            | EUR (Oct<br>2021)      | Total Social<br>Costs; Disability<br>Pension Costs               | No significant difference in total<br>social costs between the exercise<br>group (RCT) and the usual care<br>group (UC) at 18 months.<br>Significantly lower disability<br>pension costs in the RCT<br>exercise group.                   | 18 months    | Social   | Exercise did not generate<br>significant differences in total<br>long-term social costs, although<br>there were savings in disability<br>pension costs. The cost of the<br>exercise intervention was higher<br>than in comparable studies. |
| Bruce et al.,<br>2021<br>United<br>Kingdom              | GBP<br>(2015)          | Use of secondary<br>care resources<br>(inpatient,<br>outpatient) | Uncertainty in cost-effectiveness<br>estimates was driven by the large<br>and variable costs of other<br>cancer treatments (e.g. adjuvant<br>chemotherapy).  | 12 months    | NHS and<br>Personal Social<br>Services           | By eliminating the costs of other<br>cancer treatments, the likelihood<br>of the intervention being cost-<br>effective increased significantly.  |
| Edmunds et<br>al., 2020<br>Australia and<br>New Zealand | AU\$<br>(2018)         | Intervention Cost;<br>Incremental Cost                           | Cost of physical activity<br>intervention over 6 months<br>(health care payer perspective):<br>AU\$550. Incremental cost of<br>intervention (vs. usual care):<br>AU\$546. Incremental cost<br>(societal perspective in SA):<br>AU\$1012. | 6 months     | Health Care<br>Payer (Insurer)                   | No evidence was found to<br>support cost savings in<br>subsequent resource use<br>(medicines, health services) or<br>productivity losses.  |
| Gordon et<br>al., 2017<br>Australia                     | AU\$<br>(2014)         | Incremental<br>Cost-<br>Effectiveness<br>Ratios (ICERs)          | Report ICERs in AU\$ 2014. (E.g.:<br>Cost per QALY earned \$90,842<br>in the Private EP model,<br>\$105,231 in the Service Provider<br>- Base Case model).   | 12 months    | Broad<br>(providers,<br>patients,<br>government) | Usual care dominates (less<br>costly, more effective) in some<br>sensitivity analysis scenarios.   |

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| Ucar<br>Physical Activity for | Australia                               | AU\$<br>(2019/20) | Incremental<br>Cost-<br>Effectiveness<br>Ratios (ICERs)<br>(model-based)         | Report ICERs in AU\$ 2019/2020<br>derived from model simulations<br>(e.g. ICER Base Case \$21,247<br>per QALY earned).  | Long term<br>(Model) | Social (implicit in<br>the costs<br>included)                      | The sensitivity analysis shows<br>the variability in the ICER<br>depending on the model<br>parameters.   |
|                               | Haines et al.,<br>2010<br>Australia     | AU\$<br>(2006)    | Average Costs<br>per Group<br>(Programme,<br>Medical Care,<br>Productivity)      | Mean (SD) cost over 6 months:<br>Intervention \$24,397 (1322),<br>Control \$24,119 (1430). Adjusted<br>cost difference €529 (95% CI -<br>3205 to 4452), not significant.  | 6 months             | Broad (includes<br>provisioning,<br>medical care,<br>productivity) | The intervention had higher<br>costs in medical care, but<br>significantly lower costs in<br>unpaid productivity and informal<br>care.                         |
|                               | May et al.,<br>2017<br>Netherlands      | EUR<br>(2011)     | Average Total<br>Costs (Societal,<br>Health Care) by<br>Group                    | Breast Cancer: Societal<br>Intervention €25,105 (SD<br>10,403), Societal Control €22,215<br>(SD 8652). Incremental<br>(Intervention-Control) €2912.<br>Colon Cancer: Societal<br>Intervention €21,086 (SD 7037),<br>Societal Control €25,391 (SD<br>7131). Incremental (Intervention-<br>Control) - €4321. Cost per<br>exercise session per patient:<br>€22.18. | 9 months             | Social (health<br>care)  | Cost-effective and dominant<br>(cheaper, more effective) for<br>colon cancer. Not cost-effective<br>for breast cancer (higher costs<br>with no clear effects). |
|                               | Mewes et al.,<br>2015<br>Netherlands    | EUR<br>(2010/11)  | Intervention<br>Costs; Total<br>Costs (5-year<br>model);<br>Incremental<br>Costs | Intervention costs: CBT €190, EP<br>€197. Total costs over 5 years:<br>CBT €2,983, PE €2,983, WLC<br>€2,798. Incremental Costs (vs<br>WLC): CBT €184, PE €185.  | 5 years<br>(Model)   | Dutch health<br>system   | CBT probably most cost-effective<br>in alleviating menopausal<br>symptoms, followed by PE.   |
|                               | Schouten et<br>al., 2025<br>Netherlands | EUR<br>(2021)     | Average Total<br>Costs by Group;<br>Adjusted<br>Difference                       | Average Total Costs: CG €9,700,<br>EG (1:1) €9,568, EG (1:4)<br>€8,482. Adjusted Difference (EG<br>vs CG): -€163 (1-to-1), -€1,249<br>(1-to-4).   | 9 months             | Social   | The supervised exercise (both<br>1:1 and 1:4) was dominant (more<br>effective and less costly) from a<br>societal perspective.                                 |

| J                             | 0   |               |   |   |                        |        |  |
|-------------------------------|---|---------------|---|---|------------------------|--------|--|
| Ucar<br>Physical Activity for | Van Dongen<br>et al., 2019<br>Netherlands | EUR<br>(2014) | Cost of<br>Intervention per<br>Patient; Average<br>Total Costs per<br>Group | Intervention cost per patient:<br>€1340. Average Total Costs:<br>Intervention €24,397, Control<br>€24,119. Adjusted cost difference<br>€529 (95% CI -3205 to 4452), not<br>significant. | >1 year<br>(follow-up) | Social | Total social costs were higher in<br>the intervention group but the<br>difference was not significant.<br>Health care costs were<br>significantly higher in the<br>intervention group, but unpaid<br>productivity and informal care<br>costs were significantly lower. |

#### Abbreviations:

AU\$: Australian dollar; CBT: cognitive behavioural therapy; CG: control group; EG: experimental group; EUR: euro; ICERs: incremental cost-effectiveness ratios; NHS: National Health Service; PE: physical exercise; QALYs: quality-adjusted life-years; RCT: randomised controlled trial; SD: standard deviation; UC: usual care; WLC: waiting list control.

#### 4. Conclusions

This report aimed to synthesise the current evidence on the cost-effectiveness of exercise therapy in the cancer population. A total of ten economic evaluations performed from 2010 to 2025 were included.

Overall, the economic analyses presented vary considerably in their scope, methodology and results. Although the evidence is still inconclusive, some studies suggest that exercise for cancer may be cost-effective or even dominant in certain populations and contexts (e.g., colorectal cancer, metastatic breast cancer), with the costs of the intervention offset by savings in health care or productivity (particularly reduced long-term disability pensions). Other studies found no significant cost savings or cost-effectiveness in different populations or with shorter time horizons.

In conclusion, although considerable efforts have been made to evaluate the economic aspects of exercise in oncology, the current scarcity of economic studies, along with the heterogeneity of their methodologies, study populations and time horizons, makes it difficult to draw general conclusions or directly compare the reported cost-effectiveness. Evidence suggests that the economic impact may be variable, depending on factors such as the type of cancer, the timing of the intervention and the extent of the costs considered (social vs medical care perspective). Finally, it is recommended that future economic evaluations on this topic be conducted, as they can provide valuable insights and inform policy decisions.



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#### Supplementary material

 Table S1. List of excluded records with reasons.

| Rea  | son 1. Control group received exercise intervention (C).   |
|------|--|
| 1.   | Watzek JT, Gordon LG, Sandler CX, Spence RR, Vagenas D, Pyke C, Hayes SC. A cost-consequences analysis of the SAFE trial: a comparative, effectiveness trial evaluating high- versus low-supervision of an exercise intervention for women with breast cancer. Breast Cancer. 2023 Mar;30(2):249-258. doi: 10.1007/s12282-022-01418-1.   |
| 2.   | Ax AK, Husberg M, Johansson B, Demmelmaier I, Berntsen S, Sjövall K,<br>Börjeson S, Nordin K, Davidson T. Cost-effectiveness of different exercise<br>intensities during oncological treatment in the Phys-Can RCT. Acta Oncol. 2023<br>Apr;62(4):414-421. doi: 10.1080/0284186X.2023.2200149.   |
| 3.   | Alibhai SMH, Papadopoulos E, Mina DS, Ritvo P, Tomlinson G, Sabiston CM,<br>Durbano S, Bremner KE, Chiarotto J, Matthew A, Warde P, O'Neill M, Culos-<br>Reed SN. Home-based versus supervised group exercise in men with prostate<br>cancer on androgen deprivation therapy: A randomized controlled trial and<br>economic analysis. J Geriatr Oncol. 2024 Jan;15(1):101646. doi:<br>10.1016/j.jgo.2023.101646. |
| 4.   | Kampshoff CS, van Dongen JM, van Mechelen W, Schep G, Vreugdenhil A,<br>Twisk JWR, Bosmans JE, Brug J, Chinapaw MJM, Buffart LM. Long-term<br>effectiveness and cost-effectiveness of high versus low-to-moderate intensity<br>resistance and endurance exercise interventions among cancer survivors. J<br>Cancer Surviv. 2018 Jun;12(3):417-429. doi: 10.1007/s11764-018-0681-0.                               |
| 5.   | van Waart, H., van Dongen, J. M., van Harten, W. H., Stuiver, M. M., Huijsmans, R., Hellendoorn-van Vreeswijk, J. A. J. H., Sonke, G. S., & Aaronson, N. K. (2018). Cost-utility and cost-effectiveness of physical exercise during adjuvant chemotherapy. The European journal of health economics: HEPAC: health economics in prevention and care, 19(6), 893–904. doi: 10.1007/s10198-017-0936-0.             |
| Rea  | son 2. Multimodal intervention or exercise intervention does not meet our  |
| sele | ection criteria (I).   |
| 6.   | Perrier L, Foucaut AM, Morelle M, Touillaud M, Kempf-Lépine AS, Heinz D,<br>Gomez F, Meyrand R, Baudinet C, Berthouze S, Reynes E, Carretier J,<br>Guillemaut S, Pérol D, Trédan O, Philip T, Bachmann P, Fervers B. Cost-<br>effectiveness of an exercise and nutritional intervention versus usual nutritional<br>care during adjuvant treatment for localized breast cancer: the PASAPAS                      |



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