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SYSTEMATIC REVIEW

The Cost-Effectiveness of Adjunctive Lifestyle Interventions for the Management of Cancer: A Systematic Review

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Abstract

Objective There is a paucity of papers synthesizing the cost-effectiveness (CE) of lifestyle interventions to support cancer patients, and the synthesis papers available have used analytic methods that do not permit easy comparison between studies. We therefore evaluated the CE of adjunctive lifestyle interventions compared with usual care.

Methods A systematic literature search of Scopus, MEDLINE, EMBASE, PsycINFO, CINAHL and the Cochrane Library databases was conducted from database inception until June 2021. Eligible studies were economic evaluations from randomised controlled trials or modelled economic evaluations that recruited subjects with a confirmed diagnosis of cancer and were allocated to a lifestyle intervention as an adjunct or supportive treatment, or usual care. Studies were excluded if there was no cost-effectiveness analysis or if costs were identified but not related back to measures of effectiveness. CE of the included interventions was recalculated, adjusting for key differences (with respect to absolute resource costs and timing) between the broad range of study settings and a common 'target' setting. All CE data were converted into incremental net monetary benefit using a common cost-effectiveness threshold to facilitate comparison. The quality of the studies was evaluated for risk of bias using the ECOBIAS check list.

Results Nine studies were included in our review. Seven studies investigated the benefits of physical exercise in combination with cancer treatment and two studies investigated the combination of exercise and psychosocial counselling alongside cancer treatment. Six studies with an exercise intervention reported larger quality-adjusted life year (QALY) gains compared with usual care and when cost per QALY gained was considered, three of the interventions were cost effective. One of the two interventions combining exercise with psychosocial counselling was cost effective. All studies were considered of good quality but all had some limitations.

Conclusions The evidence to support the cost effectiveness of lifestyle interventions in patients with cancer is mixed with four of the nine interventions found to be cost effective and two remaining cost effective when uncertainty was taken into account. Sensitivity analysis showed the influence of the CE threshold on the results, highlighting the importance of selecting a CE threshold that is appropriate to the setting.

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Key Points for Decision Makers

Lifestyle interventions may improve outcomes in cancer patients but there is a paucity of papers synthesising whether it is cost effective to do so.

Incremental net monetary benefit overcomes some barriers to synthesising results from cost-effectiveness analyses and drawing conclusions for a 'target' setting.

Using the Australian setting as an example, there is mixed evidence demonstrating that lifestyle interventions may be a cost-effective option for improving outcomes in cancer patients.

1 Introduction

Cancer is a leading cause of death, and worldwide there are an estimated 19.3 million new diagnoses and almost 10 million deaths attributable to the disease each year [1]. Cancer is recognised as a chronic disease, and like other chronic conditions, it is associated with progression over time, long duration, and involves lengthy treatment periods. These factors combine to negatively impact on patients' quality of life, lower functional status and productivity, as well as increase healthcare costs [2]. Treatment for cancer typically focuses on improving survival rates, but rehabilitation of physical function and improvements in quality of life may be required for health maximisation (both at the individual level and at the societal level).

Lifestyle factors (e.g. obesity, tobacco use) can increase the risk for developing cancer, but equally, modifying negative behaviours can lead to potential health gains [3]. The benefits of lifestyle interventions for cancer patients are summarised in several systematic reviews [4–8]. The Australian Association of Exercise and Sport Science recommends regular low-moderate intensity exercise for people undertaking or having completed cancer treatment as it can optimize cancer outcomes [9], an opinion supported by a consensus statement from an international, multidisciplinary roundtable convened by the American College of Sports Medicine [10]. Exercise is recommended in both adult and paediatric populations as both adults and childhood cancer patients decrease their physical activity during cancer treatment, which can exacerbate adverse events [11]. Whilst it is less well studied than in adult populations, there is some evidence of a positive effect of physical activity on physical well-being, organ function and fatigue in children during and after cancer treatment [12–14]. The American Cancer Society further publishes guidelines for nutrition and physical exercise to educate healthcare providers and to help patients make evidence-based choices related to nutrition and exercise—from diagnosis, through treatment, and on to remission [15].

There are two key issues that currently limit the ability of decision-makers to evaluate if it is cost effective to use lifestyle interventions in support of cancer populations undergoing treatment. First, there is a paucity of papers synthesising the current evidence base of economic evaluations in this field. Second, the synthesis papers that are available [16, 17] explore psychosocial interventions in isolation and have used analytic methods that did not permit comparison between studies.

The aim of this paper is to summarise evidence regarding cost effectiveness in a manner that will allow decision makers facing local budgetary constraints and local cost-effectiveness thresholds to more readily draw comparisons between treatments.

2 Methods

The review protocol was developed in line with the PRISMA-P guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses [18, 19]. The literature search (described below) was conducted across six databases (detailed below), from their inception up until June 2021, and registered on the PROSPERO database (CRD42020185376).

2.1 Eligibility Criteria

Eligible studies were economic evaluations arising from randomised controlled trials (RCTs) or modelled economic evaluations that recruited subjects (adults and children) who had a confirmed diagnosis of cancer (no limitations on type) and were allocated to a lifestyle intervention as an adjunct treatment or supportive treatment to improve patient outcomes or to usual care (groups pooled and evaluated based on intervention type separately). For this review, lifestyle interventions were defined as a non-pharmaceutical intervention that utilized exercise or diet, and included specialty diets, the use of dietary supplements, exercise regimes, concomitant counselling (supportive and patient guidance) with diet/exercise, and e-health technologies for delivery of a lifestyle intervention or to aid compliance to treatment (primary cancer or supportive lifestyle therapy). The studies were included if they compared the lifestyle intervention in combination with usual care or with usual care alone (see Table 1 for PICO (Population, Intervention, Control, Outcome) eligibility criteria). Usual care was selected as comparator treatment as the term "best current therapy" or

Table 1 PICO (Population, Intervention, Control, Outcome) table of eligibility criteria

PICO	Description
Participants	Patients with a confirmed diagnosis of a malignant neoplasm/cancer. Studies addressing both adults and children will be included
Intervention	Studies that have investigated the use of a lifestyle intervention as an adjunct treatment or supportive treatment to improve patient outcomes. Eligible treatments include: exercise, diet, psychosocial counselling used alongside exercise/diet, e-health technologies for delivery of a lifestyle intervention or to aide compliance
Comparison	Usual care or standard care
Outcome	Cost-effectiveness outcomes in the form of ICER or INMB

"standard of care" can lead to an inaccurate determination that there is a uniform and standardised treatment regime that is proven effective. In the absence of clinical evidence that demonstrates superiority of one practice over another, usual care may encompass a wide variety of treatment practices. In some instances, it may be a standardised treatment therapy with significant levels of clinical evidence, whilst in other conditions, the treatments used may be highly variable [20]. Studies were considered as having applied usual care if the control treatment was described as usual care with details on the treatment provided for the control arm. For this review, economic evaluations were classified as comparative analyses of alternative interventions with regard to the cost of delivering the treatment, the cost of other resources used, and the health outcomes in the form of increases in quality-adjusted life years (QALYs). The findings of the economic evaluation should be reported in the form of an ICER (incremental cost-effectiveness ratio) or INMB (incremental net monetary benefit) of the intervention compared with usual care. There were no restrictions based on type of setting but only studies reported in English were considered.

Studies were excluded if there was no cost-effectiveness analysis or if costs were identified but were not related back to eligible measures of effectiveness (i.e. QALYs). Studies that described methodological approaches, protocols and review articles were excluded. Studies that were not peer-reviewed or published in a journal were excluded.

2.2 Search Strategy and Data Extraction

A systematic literature search of Scopus, MEDLINE, EMBASE, PsycINFO, CINAHL and the Cochrane Library electronic databases was conducted from their inception to June 2021. The search strategy was created in conjunction with a health sciences librarian with experience in systematic review searching. Relevant keywords and medical subject headings for population, intervention, comparison, and outcome (PICO framework) were defined and included variations (spelling, plural, etc.) and combinations of keywords. The full search strategy for Scopus is provided below, with the strategy being adapted for use with other citation databases.

(TITLE-ABS-KEY ("Cancer" OR "malignant neoplasm*" OR "tumour*" OR "tumor*")) AND (TITLE-ABS-KEY ("usual care" OR "routine care")) AND ((TITLE-ABS-KEY ("exercise" OR "sports" OR "physical activity" OR "training" OR "yoga")) OR (TITLE-ABS-KEY ("diet" OR "fasting" OR "dietary supplement" OR "food supplement")) OR (TITLE-ABS-KEY ("counsel*" OR "guidance" OR "motivational interview*" OR "e-counsel*" OR " patient guidance" OR "tele-counsel*" OR "e-therapy" OR "tele-therap*" OR "e-counsel*" OR "tele-counsel*" OR "cognitive therap*")) OR (TITLE-ABS-KEY ("stress management" OR "meditation" OR "yoga" OR "tai-chi" OR "health behavio*"))) AND ((TITLE-ABS-KEY ("cost effective* analys*" OR "cost benefit analys*" OR "cost utilities analys*" OR "cost effectiveness" OR "cost benefit" OR "cost utility")) OR (TITLE-ABS-KEY ("qaly*" OR "daly*" OR "net benefit*" OR "net health benefit*" OR "quality adjusted life year*" OR "disability adjusted life year*")))

The reference lists of the identified studies and systematic reviews were screened manually for any relevant studies that were not identified in the electronic database search.

Citations and abstracts were imported into EndNote X9 citation manager and were then exported into Covidence (www.covidence.org), a cloud-based systematic review management application, for removal of duplicates and screening. Title and abstract screening were conducted by the lead author (AG) and ineligible references such as case reports, conference abstracts and protocols, and duplicates published in different journals were removed. Potentially eligible full-text studies were screened by two reviewers (AG, VS) against the inclusion/exclusion criteria. Any disagreements were discussed and considered resolved when a consensus on the study eligibility was reached.

Data were extracted into a predefined spreadsheet and the following information was recorded: study identification number; corresponding author and email address, title of paper, publication year, institute, study design, inclusion criteria, exclusion criteria, participant details (number of subjects randomised to groups, mean age, gender, condition-specific characteristics), treatment details, control details,

clinical health outcomes, QALY outcomes, scope of cost-analysis (direct medical costs, direct non-medical costs, indirect non-medical costs), economic characteristics (reported currency, cost reference year, discount rate, funding threshold), main results (point estimates, confidence intervals, variance, standard errors for total cost, QALYs, ICERs, and net monetary benefit), sensitivity analyses (methods and results), funding sources.

2.3 Risk of Bias Assessment

There are several checklists available to evaluate the quality and risk of bias of a study [21–24]. In this review, the studies were assessed using the Bias in Economic Evaluation (ECOBIAS) checklist [21]. The ECOBIAS checklist is a contemporary 22-item list intended to improve the quality of health economic evaluations by identifying key biases that could occur in economic evaluations. The checklist includes biases for both trial-based and model-based economic assessments, with 11 trial-based evaluation items (Part A) and 11 modelling-specific items (Part B). For the purposes of assessing the risk of bias in this analysis, two studies [25, 26] were evaluated using both Part A and Part B as they included a modelled extrapolation of trial data. The other seven studies were trial-based economic evaluations and were evaluated with Part A alone of the ECOBIAS checklist. Alongside Part A of the ECOBIAS checklist, we used the detailed descriptions of trial-based biases described in Evers et al. to aid assessment [27]. Evers et al. discussed the source and mitigation strategies for the same 11 biases that were subsequently included in the ECOBIAS list. The included studies were independently assessed for bias by two reviewers (AG, VS), with any differences in opinion discussed until a consensus was reached.

2.4 Data Analysis and Synthesis

Due to the heterogenous nature of the patient populations, cancer types, usual care treatment, health outcomes, costs and resource use in the included studies, the use of meta-analysis to compare cost effectiveness was not appropriate. Consequently, the cost effectiveness of the treatments was compared through a narrative synthesis and the studies were grouped based on type of intervention (exercise/counselling/combination of both).

As the context for this analysis was the Australian setting, all costs were converted into Australian dollars using the interbank exchange rates from the Reserve Bank of Australia taken last banking day for the cost reference year [28]. To mitigate confounding cost variables, all the costs were adjusted for inflation and purchasing power parity using the Consumer Price Index data from the World Bank [29] and Organisation for Economic and Co-operation and Development (OECD) [30]. All cost-effectiveness values were reported in 2020 Australian dollars. One paper [31] did not report a cost reference year and so the reference year was assigned as the year the last patient completed their final clinic visit.

The quality of reporting in the studies was assessed by two reviewers (AG and VS) using the Consolidated Health Economic Evaluating Reporting Standards (CHEERS) checklist [23]. Studies were screened using the checklist for the presence of all items recommended for inclusion in an economic evaluation of a health intervention.

Many economic evaluations of healthcare products report their findings in the form of an ICER. However, there are methodological limitations with the ICER such as the interpretation of negative ICERs and the construction and interpretation of confidence intervals [32, 33]. In response to these limitations, alternative methods have been developed and the INMB is one such method [34–36]. INMB compares costs and benefits on the common scale of dollar-values and classical statistical methods can be used to construct confidence intervals from the sample mean and variance. Some advantages of INMB are that it can be used to quantify value across many (health, education, environmental) outcomes of interest. As INMB is expressed in monetary terms, it also allows for comparisons of treatments applied to different patient populations where different (clinical) units of effectiveness may have been used, or for comparing public policy measures across different sectors or sub-sectors of the economy [35].

The primary outcome in this review was the INMB, and it was calculated for each study as follows:

$$b(\lambda) = \lambda \times \Delta E - \Delta C \tag{1}$$

where $b(\lambda)$ is the INMB, λ is the cost-effectiveness threshold, ΔE is the difference in effectiveness, and ΔC is the difference in costs.

The use of INMB as a function of λ when reporting cost effectiveness is beneficial as it allows a reader to use a cost-effectiveness threshold that is appropriate to them; however, there is debate about the best way to measure the cost-effectiveness threshold, or even if a threshold should be used, and, if so, what it should represent and how to derive its value [37–41]. There are two main cost-effectiveness threshold perspectives: demand-side estimates that reflect the value society places on healthcare gains, and supply-side estimates that reflect the opportunity cost resulting from required disinvestment in another technology in order to adopt a new one [40]. The demand-side approach attempts to link cost-effectiveness analysis with cost-benefit analysis and welfare economics, and is useful when the healthcare budget can expand in line with societal willingness to pay to accommodate new technologies.

In situations where the budget is fixed or constrained, funding new technologies will require disinvestment from existing treatments and a supply-side threshold is more appropriate. Supply-side thresholds reflect the cost per QALY of displaced services [38]. Both demand-side and supply-side thresholds are context-specific, reflecting local preferences in the case of demand-side thresholds and local arrangements for delivery and finance of healthcare in the case of supply-side thresholds. This highlights an important aspect of cost-effectiveness analysis in that the target context needs to be considered for optimal resource allocation.

This review is using the Australian setting as an example and so a threshold value (λ) appropriate to the Australian setting was required. Because Australia operates within a constrained healthcare budget, a supply-side estimate of the cost-effectiveness threshold was used. A recent supply-side estimate reported by Edney et al. [38], adjusted for inflation (AU$28,033 original value, adjusted to 2020 AU$28,723), was therefore chosen as the value of λ for this analysis.

The potential of INMB to facilitate quantitative synthesis of economic evidence is frequently mentioned but rarely implemented [42]. This potential is limited by (i) barriers to comparability and transferability, and (ii) data requirements and statistical issues. The present paper tests the feasibility of overcoming some of these issues by using Australia as an example, converting costs into 2020 Australian dollars, and then using an empirically derived estimate of the Australian funding threshold (inflated to 2020 AUD) to calculate INMB. This approach directly addresses some of the key barriers to transferability identified by Sculpher et al. [43], Welte et al. [44], and Shields and Elvidge [42].

2.5 Sensitivity Analysis

In Australia, there is currently no clear pathway to government funding via the Pharmaceutical Benefits Advisory Committee (PBAC) or the Medical Services Advisory Committee (MSAC) for lifestyle treatments, many of which may be most efficiently delivered by providers who would be ineligible for a Medicare Provider Number. There is, however, a responsibility for government fund-holders to maximise population health. We therefore additionally assessed cost effectiveness using a demand-side threshold as calculated by Shiroiwa et al. [39] (AU$64,000, adjusted to AU$79,569 to account for inflation), to simulate an expansion of the healthcare budget for the Australian setting. We also evaluated cost effectiveness for a cost-effectiveness threshold of AU$0, to simulate programmes that require new proposals to be cost neutral.

To evaluate the uncertainty around the INMB, 95% confidence intervals were calculated for the different cost-effectiveness thresholds selected. To calculate the confidence intervals, the variance of INMB was estimated as follows:

$$\text{var}[b(\lambda)] = \lambda^2\sigma^2_{\Delta E} + \sigma^2_{\Delta C} - 2 \times \lambda \times \rho_{\Delta C,\Delta E}\sigma^2_{\Delta E}\sigma^2_{\Delta}, \quad (2)$$

where var$[b(\lambda)]$ is the variance of INMB, λ is the cost-effectiveness threshold, $\sigma^2_{\Delta E}$ is the variance of the difference in effectiveness, $\sigma^2_{\Delta C}$ is the variance of the difference in costs, and $\rho_{\Delta C,\Delta E}$ is the correlation coefficient for ΔC and ΔE. Economic studies can report many different parameters, and the recommendations of Bagepally et al. [45] were followed to obtain the requisite data to estimate the variance of INMB. Bagepally et al. describe five potential scenarios relating to data availability, three of which were applicable to the studies included in this analysis and are described below:

Scenario 1: Point estimates and variances for every parameter are reported and variance of INMB is calculated directly using Eq. (2). This scenario was applied to one study [46].

Scenario 2: Studies do not report sufficient dispersion data but provide the cost-effectiveness plane (CE-plane) scatter plot. Individual values of ΔC and ΔE are manually extracted from the CE-plane using Web-Plot-Digitizer software [47]. Means of ΔC and ΔE and their variances and covariances can be estimated accordingly, allowing variance of INMB to be estimated using Eq. (2). This scenario was applied to four studies [25, 48–50].

Scenario 3: The study does not report sufficient dispersion data nor the CE-plane but only provides point estimates of ΔC and ΔE and the ICER. In these situations, measures of dispersion are substituted from similar studies, providing the type of cancer, type of intervention, stratum of country income, and the ICERs are not significantly different (± 50–75%) allowing the variance of INMB to be estimated using Eq. (2). This scenario was applied to four studies [17, 26, 31, 51].

Variance of INMB was further inflated/deflated to test sensitivity to alternative assumptions/estimates of sampling error, with the variance of INMB either being inflated by 1.5 or deflated by 0.67.

Net monetary benefit graphs were plotted for each study for visual appraisal, and x-axis intercepts calculated for INMB, and lower 95% confidence limits (calculated under alternative assumptions regarding the extent of sampling error). The x-intercept of the lower CI limit represents the cost-effectiveness threshold above which we can be 95% confident that the treatment is good value.

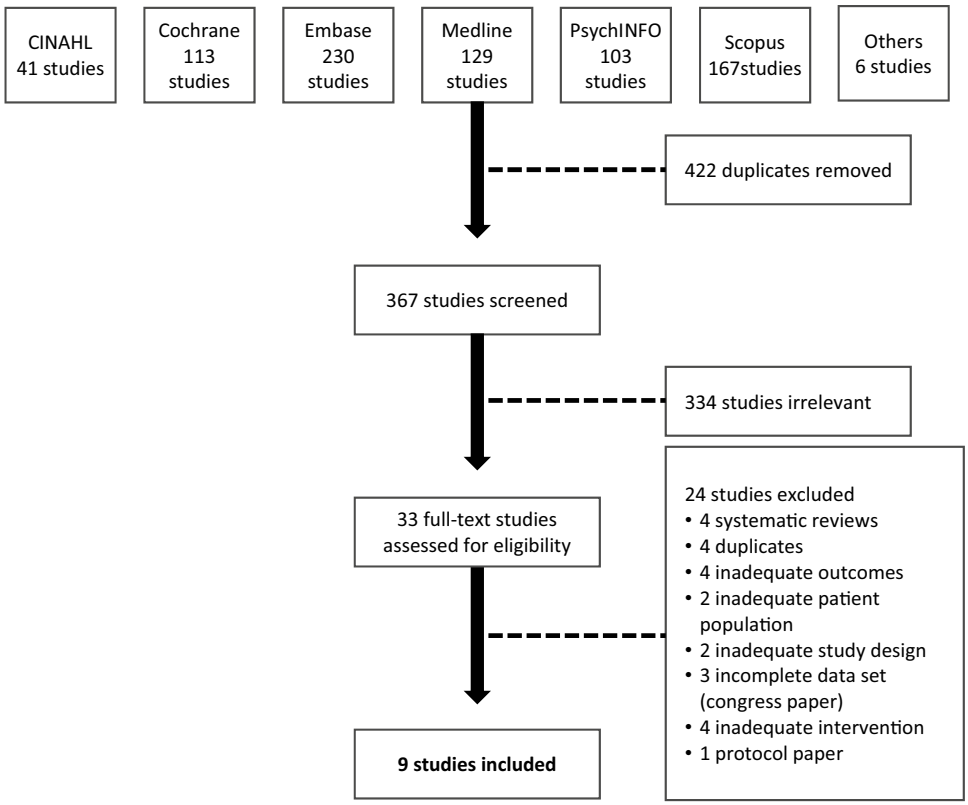

Fig. 1 Flow chart of study selection

3 Results

The results of the literature search and selection process are summarised in Fig. 1. The search was conducted in June 2021 and yielded 789 records, of which 422 were duplicates and were removed. During title and abstract screening, a further 334 studies were removed as not meeting the inclusion criteria, leaving 33 studies for full-text assessment. After assessment of the full text, nine studies were included in our review. Twenty-four studies were excluded: four were excluded as they were systematic reviews rather than RCTs, four were duplicates, four studies had the incorrect outcome (e.g. costs not related to QALYs gained/lost), two were excluded as the studies were conducted in the incorrect patient population, two studies had a study design that did not match the inclusion criteria, three studies had incomplete data set as they were congress papers, four studies had an intervention that did not match the inclusion criteria, and one study was excluded as it was a protocol paper. Studies were grouped by type of intervention into exercise or exercise combined with psychosocial counselling.

3.1 Included Studies: Characteristics

The characteristics of the included studies are summarized in Table 2. Of the included studies, four were conducted in The Netherlands [25, 48, 50, 51], three studies were conducted in Australia [46, 49, 52], and two were conducted in the USA [26, 31]. Three of the studies investigated lifestyle interventions in subjects with breast cancer [46, 51, 52], two studies recruited subjects with prostate cancer [31, 49], one study recruited subjects with squamous cell carcinoma within the oral cavity (oropharynx, hypopharynx, larynx or nasopharynx) [25], and one study recruited subjects with a range of paediatric cancers including haematological malignancy, brain and CNS tumours, and other solid cancers [48]; one study recruited subjects with lung cancer [26]; and one recruited subjects with mixed cancer types (breast and colon cancer [50]). Eight of the studies were in an adult population whilst one was in a paediatric population [48].

3.2 Study Design

Four of the studies were two-arm RCTs that investigated a single lifestyle intervention compared with usual care [46, 48–50], three of the studies were multi-arm RCTs and compared usual care with two related lifestyle interventions [31, 51, 52], one study used a decision-analytic model that pooled the data from two two-arm RCTs that followed the same protocol and compared a single lifestyle intervention compared with usual care [25], and the final study used Markov modelling to estimate the cost effectiveness of a lifestyle intervention from a large multicentre clinical study [26]. Seven of the studies investigated the benefits of

Table 2 Characteristics of the included studies

Study (publication year)	Country	Age, y	Cancer type	Design	Intervention	Time horizon	Currency year	Perspective	Sensitivity analysis
Braam et al. (2017) [48]	Netherlands	13.3	Haematological malignancy, brain and CNS tumour, other solid cancer	2-arm RCT $n=68$	Exercise + psycho-social training	12 months	2011	Societal perspective	One-way Additional exercise Different efficacy test Healthcare perspective costs PSA with CEAC and CE-plane provided
Edmunds et al. (2020) [49]	Australia	72	Prostate cancer	2-arm RCT $n=100$	Exercise	12-months	2018	Healthcare perspective	One-way Vary effect size Societal perspective costs Varying costs based on number of participants Maintenance of QoL after exercise programme PSA with CEAC and CE-plane provided
Gordon et al. (2017) [52]	Australia	52.4	Breast cancer	3-arm RCT $n=194$	Exercise	12 months	2014	Healthcare perspective	One-way Different cost models PSA
Ha et al. (2020) [26]	USA	70	Lung cancer	Markov model to estimate the cost-effectiveness from a large multicentre RCT $n=1635$	Exercise	5 years	2017	Societal perspective Organizational perspective	One-way Varying costs Probability of increasing exercise Health utility benefit of exercise PSA with CEAC provided
Haines et al. (2010) [46]	Australia	56	Breast cancer	2-arm RCT $n=89$	Exercise	6 months	2009	Societal perspective	One-way Excluding outliers PSA with CE-plane provided
May et al. (2016) [50]	Netherlands	60.0	Breast cancer or colon cancer	3-arm RCT $n=237$	Exercise	36 weeks	2011	Societal perspective Healthcare perspective	One-way Differences in disease state Exclude non-healthcare costs Vary costs (higher/lower) PSA with CEAC and CE-plane provided

Table 2 (continued)

Study (publication year)	Country	Age, y	Cancer type	Design	Intervention	Time horizon	Currency year	Perspective	Sensitivity analysis
Retel et al. (2011) [25]	Netherlands	60.0	Advanced head and neck cancer	Decision-analytic model that pooled the data from two 2-arm RCTs $n = 90$	Exercise	24- months	2008	Healthcare perspective	One-way Changes in utility estimates Changes in costs (higher/lower) PSA with CEAC and CE-plane provided
van Waart et al. (2017) [51]	Netherlands	50.7	Breast cancer	3-arm RCT $n = 230$	Exercise	12 months	2017	Societal perspective	One-way Completed cases only Variations in costs (human capital approach, frictional cost approach, planned sessions vs. attended, excluded non-healthcare costs, time-cost of patients) PSA with CEAC provided
Zhang & Fu (2016) [31]	USA	64.8	Prostate cancer	3-arm RCT $n = 267$	Exercise + psycho-social training	6 months	2013	Societal perspective Provider perspective Patient perspective	None reported

CEAC cost-effectiveness acceptability curve, *CE-plane* cost-effectiveness plane, *PSA* probabilistic sensitivity analysis

physical exercise [25, 26, 46, 49–52] in combination with cancer therapy, and two studies investigated the benefits from a combination of physical exercise and psychosocial support [31, 48] whilst undergoing treatment for cancer. All of the studies compared the lifestyle intervention to usual care. QALYs was the metric used to evaluate effectiveness of the intervention in all included studies. The sample size for the economic analyses varied from 68 subjects to 1635 subjects. The majority of studies reported power calculations for sample size (either in the economic analysis paper or in previously published methods/results papers), and those that did not were economic modelling studies [25, 26]. The follow-up period for the studies varied between 6 months to 5 years, with two studies having a 6-month follow-up [31, 50], five studies having a 12-month follow-up [46, 48, 49, 51, 52], one study reporting a 24-month follow-up [25], and one study having a 5-year follow-up period [26].

3.3 Costs

The selected studies were conducted from a range of perspectives. Six studies [26, 31, 46, 48, 50, 51] evaluated cost-effectiveness from the societal perspective, which included intervention costs, the direct and non-direct medical costs associated with the illness and delivery of treatment, as well as direct and indirect non-medical costs such as productivity losses, travel costs, informal care, etc. All the studies considered and included relevant medical costs associated with their treatment; however, not all the studies considered all of the relevant non-medical costs, with travel costs being the most frequently omitted, even though patients were required to travel for treatment. The remaining three studies [25, 49, 52, 53] conducted cost-effectiveness analyses from the healthcare perspective, which only included intervention costs and direct and indirect medical costs.

3.4 Risk of Bias Assessment

The results of the risk of bias assessment are summarized in Table 3. Five of the included studies [31, 46, 48, 50, 51] considered costs from the societal perspective for their primary analysis, with the other four studies [25, 26, 49, 52] using the healthcare perspective (one of these studies included partial societal perspective in a sensitivity analysis [49]). It is generally recommended that cost-effectiveness analyses consider costs from the societal perspective, but the healthcare perspective may be more appropriate when the resource allocation decision is solely focused on the optimal allocation of a healthcare budget. In two of the three studies that used the healthcare perspective, this was justifiable as the studies took place in Australia where the competent authority requires evaluations from a healthcare perspective for base- or reference-case analyses [54, 55]. The suitability of the choice of healthcare perspective in one study [25] was not clear. This study was conducted in the Netherlands, where the national guidelines for conducting economic assessments in healthcare recommend the use of a societal perspective for cost-effectiveness analyses [56]. The paper was an economic modelling study and so societal costs could have been simulated; however, no explanation was provided on the choice of perspective, so it is unclear if any relevant costs have been omitted. Evaluation from a healthcare perspective may limit the usefulness of results as it would make comparison difficult against other technologies that have been evaluated from a broader perspective.

All the studies used an appropriate ‘current practice’, usual cancer care in combination with the lifestyle intervention and compared the outcomes with usual care alone.

The studies generally considered and identified relevant costs, although two studies [48, 51] did not consider travel costs that were relevant, and one study did not include resource use during the follow-up period [52]. All the studies presented their cost calculations in a detailed manner, making use of reference prices, and cardinal scales were used in all the studies for the outcome measures. Two studies [25, 26] applied discounting to future costs, and it was appropriate for the remaining studies to not discount costs as the duration of follow-up was less than 12 months.

Double counting is a potential bias but debate regarding double counting of productivity costs remains unresolved [57]. Double counting may arise when cost-utility analyses are conducted from a societal perspective as productivity gains/losses may be captured in both the cost side of the equation as well as the outcomes side when QALYs are used as the outcome measure [58–60]. Recent guidelines [57] recognise the possibility of double-counting but recommend inclusion of (unadjusted) productivity costs in base-case analyses. Robustness to double-counting bias can then be demonstrated via sensitivity analyses that exclude productivity costs. All of the reviewed studies that evaluated costs from the societal perspective potentially suffered from this bias as they included productivity costs and used QALYs as the outcome but made no attempt to demonstrate robustness to double-counting bias (i.e., productivity losses excluded in sensitivity analysis).

The majority of the studies considered methodological and structural uncertainty and heterogeneity, and tested their results through sensitivity analyses; however, one study did not conduct sensitivity analyses [31]. Additionally, two studies only partially explored uncertainty: one study did not consider the impact of heterogeneity due to the different cancer types included in their analysis [48], and one study only considered the impact of extreme outliers in the analysis and did not explore uncertainty around other parameters [46]. All of the studies disclosed their source of funding and there were no industry funding sources. The registration of

Table 3 Risk-of-bias assessment using the ECOBIAS checklist

	Braam et al., 2017 [48]	Edmunds et al., 2020 [49]	Gordon et al., 2017 [52]	Ha et al., 2020 [26]	Haines et al., 2010 [46]	May et al., 2017 [50]	Retel et al., 2011 [25]	van Waart et al., 2017 [51]	Zhang and Fu, 2016 [31]
PART A. Overall checklist for bias in economic evaluation									
Was a societal perspective adopted? If not, has a different perspective been justified?	Yes	No but justified. Societal costs in sensitivity analysis	No but justified	Yes	Yes	Yes	No. Justification unclear	Yes	Yes
Was the best alternative chosen as comparator? Was current practice chosen as a comparator? Have all comparators been described in sufficient detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Were all costs relevant to the disease and intervention identified and considered?	Partly. Did not include travel costs	Partly. Societal costs partly considered for sensitivity analysis. Did not include productivity loss costs etc.	Yes	Yes.	Yes.	Yes	Yes	Partly. Did not consider travel costs	Yes
Was the resource use measured continuously?	Yes	Yes	No. Resource use during follow-up not recorded	Yes	Yes	Yes	Yes	Yes	Yes
Is the price calculation presented in a detailed manner? Have reference prices been used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Have cardinal scales for the outcomes measure in a CEA been used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Are variables adequately checked for double-counting?	No	Yes	Yes	Partly	No	No	Yes	No	No
Have discounting rates from guidelines been applied?	N/A (study < 12 months)	N/A (study < 12 months)	N/A (study < 12 months)	Yes	N/A (study < 12 months)	N/A (study < 12 months)	Yes	N/A (study < 12 months)	N/A (study < 12 months)
Have the four principles of uncertainty (methodological, structural, heterogeneity, parameter) been considered in sufficient detail?	Partly	Yes	Yes	Yes	Partly	Yes	Yes	Yes	No
Have sponsorships been disclosed? Is the study protocol freely accessible?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Has the study/trial been listed in a trial register? Have all results been reported according to the study protocol?	Yes	Yes	Yes	N/A. Modelling study	Yes	Yes	Yes	Yes	Yes

Table 3 (continued)

	Braam et al., 2017 [48]	Edmunds et al., 2020 [49]	Gordon et al., 2017 [52]	Ha et al., 2020 [26]	Haines et al., 2010 [46]	May et al., 2017 [50]	Retel et al., 2011 [25]	van Waart et al., 2017 [51]	Zhang and Fu, 2016 [31]
PART B. Model-specific aspects of bias in economic evaluation									
I Bias related to structure									
Is the model structure in line with coherent theory? Do treatment pathways reflect the nature of disease?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
Is there an adequate comparator, i.e. care as usual?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
Is the model chosen adequate regarding the decision problem?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
Was a lifetime horizon chosen? Were shorter time horizons adequately justified?	N/A	N/A	N/A	No but adequately justified.	N/A	N/A	No but adequately justified.	N/A	N/A
II Bias related to data									
Are the methods of data identification transparent? Are all choices justified adequately? Do the input parameters come from high- quality and well-designed studies?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
Are probabilities, for example, based on natural history data? Is transformation of rates into transition probabilities done accurately?	N/A	N/A	N/A	Probabilities based on disease-free survival data from large series	N/A	N/A	Partly. No reference to applying a half-cycle correction to transitions	N/A	N/A
Are relative treatment effects synthesized using appropriate meta- analytic techniques? Are extrapolations documented and well justified? Are alternative assumptions explored regarding extrapolation?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A

Table 3 (continued)

	Braam et al., 2017 [48]	Edmunds et al., 2020 [49]	Gordon et al., 2017 [52]	Ha et al., 2020 [26]	Haines et al., 2010 [46]	May et al., 2017 [50]	Retel et al., 2011 [25]	van Waart et al., 2017 [51]	Zhang and Fu, 2016 [31]
Are the utilities incorporated appropriate for the specific decision problem?	N/A	N/A	N/A	Yes. Justifications given for use.	N/A	N/A	Unclear	N/A	N/A
Is the process of data incorporation transparent? Are all data and their sources described in detail?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
Have the four principles of uncertainty (methodological, structural, heterogeneity, parameter) been considered?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A
III Bias related to consistency									
Has internal consistency in terms of mathematical logic been evaluated?	N/A	N/A	N/A	Yes	N/A	N/A	Yes	N/A	N/A

N/A not applicable

the underlying clinical trial in a clinical trial registry could not be ascertained in one study [26].

Two of the reviewed studies [25, 26] were modelling studies and potential bias was further evaluated against an additional 11 parameters. In both studies, the structures of the models were adequate to reduce bias as they were consistent with current understanding of the disease being investigated, both used a suitable comparator, and both models were appropriate for the decision problem. Neither study considered a lifetime horizon, but in one study [26], a 5-year survival horizon was appropriate considering the age of the participants and prognosis of their disease. Similarly, the time-horizon for the other study [25] was also adequately justified as the health-related quality of life effects and costs could be adequately measured in the selected time horizon.

Both studies considered and accounted for potential bias relating to data; however, one study [25] did not apply a half-cycle correction to transitions in the model as is recommended. With the same study, there was a potential bias in the utilities used. The utilities for the usual care group were calculated from a published study [61] on the quality of life of patients treated with concomitant chemo-radiotherapy, whilst utilities for the treatment group were based on assumptions from "published literature and informal expert elicitation" with no further clarification on the underpinning assumptions. The utilities used were, however, varied during sensitivity analysis.

Overall, all of the studies met more than 70% of the ECOBIAS criteria, with four studies meeting more than 80% of the criteria [25, 46, 48, 51], and four studies meeting more than 90% of the criteria [26, 49, 50, 52].

3.5 Physical Exercise

Seven studies [25, 26, 46, 49–52] evaluated the cost effectiveness of exercise programmes on cancer outcomes (see Table 4). Gordon et al. [52], Haines et al. [46] and van Waart et al. [51] evaluated the effects of exercise compared with usual care in women with breast cancer. Edmunds et al. [49] evaluated the effects of exercise in men with prostate cancer; Ha et al. [26] investigated the effects of exercise in lung cancer patients; May et al. [50] evaluated the effects of an exercise programme in adults diagnosed with either breast or colon cancer; and Retel et al. [25] investigated the effects of specialised jaw strength and stretch exercises in patients with advanced cancer of the oral cavity, oropharynx, hypopharynx and larynx, or nasopharynx.

Six of the seven studies reported that the exercise programmes yielded larger QALY gains compared with usual care. May et al. [50] reported that the 0.026 QALY gains of their 18-week aerobic and muscle training programme came at a lower cost than usual care in patients with colon cancer (the same training programme in breast cancer groups

yielded just 0.009 QALYs), and consequently the treatment was considered dominant to usual care. In the remaining studies, however, the cost of delivering the treatment was higher than the cost of delivering usual care. For a new treatment to be considered cost effective, the cost per QALY gained should not exceed the cost-effectiveness threshold (AU$28,723 in our base-case analysis), implying a positive INMB. At this threshold, the above-mentioned dominant treatment, the preventative exercise programme of Retel et al. [25] (0.090 QALYs gained) and the moderate-high intensity exercise programme of van Waart et al. [51] (0.070 QALYs gained) were considered cost effective. If a higher, demand-side cost-effectiveness threshold was considered (AU$79,569), then the supervised resistance and aerobic exercise programme evaluated by Edmunds et al. [49] (0.009 QALYs gained) additionally had a positive INMB. For the scenario where new treatments should not add any additional cost (i.e. cost-effectiveness threshold of $0), then only the dominant treatment of May et al. [50] was cost effective when used in a colon cancer population.

3.6 Physical Exercise with Concomitant Psychosocial Counselling

Two studies evaluated the cost effectiveness of physical exercises with concomitant psychosocial counselling to teach symptom-management skills and enhance exercise participation (see Table 5). Braam et al. [48] examined the cost effectiveness of a 12-week exercise programme in a paediatric population diagnosed with childhood cancer, with six psychosocial training sessions for children and psychoeducational sessions for the parents, and Zhang and Fu [31] examined the effects of biofeedback pelvic floor exercises with concomitant psychosocial support (face to face in a group setting or support via phone) in patients with prostate cancer. Braam et al. [48] reported that the treatment yielded 0.030 more QALYs compared with usual care, whilst Zhang and Fu [31] reported 0.004 and 0.008 QALY gains for the exercise plus face-to-face or telehealth group counselling, respectively, compared with usual care.

The treatment evaluated by Braam et al. [48] returned a positive INMB at both supply side and demand side

Table 4 Cost effectiveness of physical exercise alone on cancer treatment outcomes

Study	Intervention	Cancer type	QALYs gained	Additional costs (AU$)	Incremental net benefit (AUD)		
					Supply-side threshold	Demand side threshold	Cost neutral threshold
Edmunds et al. [49]	6-month supervised exercise program (resistance and aerobic exercise)	Prostate cancer	0.009	$546	−$302	$130	−$546
Gordon et al. [52]	16 exercise sessions with physiologist. Aim exercise 4 day/week for 45 min	Breast cancer	0.009	$1036	−$778	−$320	−$1036
Ha et al. [26]	Lifestyle Interventions and Independence for Elders (LIFE) exercise intervention	Lung cancer	0.060	$7396	−$5673	−$2622	−$7396
Haines et al. [46]	Multimedia, multimodal exercise program	Breast cancer	−0.030	$8462	−$9323	−$10,849	−$8462
May et al. [50]	18-week exercise programme. Included aerobic and muscle strength training. In addition to the programme, advised to be physically active for 30 min/day for at least 3 other days per week	Breast cancer	0.009	$5992	−$5734	−$5276	−$5992
		Colon cancer	0.026	−$8926	$9673	$10,995	$8926
Retel et al. [25]	TheraBite® Jaw Motion Rehabilitation System (stretch and strength exercises with TheraBite® device)	Advanced head and neck cancer	0.090	$598	$1987	$6563	−$598
Van Waart et al. [51]	Onco-Move: Onco-Move is a home-based, low-intensity, individualized, self-managed physical activity program	Breast cancer	0.050	$4850	−$3414	−$872	−$4850
	OnTrack: OnTrack is a moderate-to-high intensity, combined resistance and aerobic exercise program		0.070	$1754	$256	$3815	−$1754

cost-effectiveness thresholds (INMB of AU$238 and AU$1763, respectively); however, in the zero-cost scenario it was not considered cost effective, with a negative INMB of AU$624.

The Zhang and Fu [31] intervention was not cost effective, as it was more costly with marginal QALY gains over usual care.

3.7 Uncertainty and Sensitivity Analysis

Variance of INMB and 95% confidence intervals were calculated. Of the nine included studies, one [46] met the criteria for scenario 1, four studies matched scenario 2 [25, 48–50], and the remaining four studies had confidence intervals calculated using scenario 3. Net monetary benefit graphs were plotted and the *x*-intercept of the lower 95% confidence limit calculated (see Online Supplementary Material (OSM)). Using the supply-side cost-effectiveness threshold, we can only conclude with 95% confidence that the interventions used in two studies were cost effective: Retel et al.'s [25] strength and stretch exercises for patients with advanced head and neck cancer (*x*-intercept AU$9622) and May et al.'s [50] exercise programme when used in colon cancer patients (treatment dominant at lower 95% CI level). Increasing the cost-effectiveness threshold as in the scenario where there is an expanding healthcare budget (demand-side threshold) did not lead to any additional studies being cost effective. In the setting where new treatments should have no additional cost, only the dominant treatment of May et al. [50] in colon patients was considered with 95% confidence to be cost effective.

A sensitivity analysis around the variance of the INMB was conducted where larger or smaller variances were used (see Table 6). The sensitivity analysis showed that when the variance was 1.5× larger than that used in the base-case analysis, there was no change in the outcomes and May et al. [50] and Retel et al. [25] were still considered cost effective at the supply-side threshold (*x*-intercepts: dominant and AU11,460 respectively). If the variance was overestimated in the base case (i.e. numerically 0.67× smaller variance used in the calculation), the moderate-high intensity OnTrack exercise intervention of van Waart et al. [51] (AU$72,836) was additionally considered cost effective with a 95% confidence when the larger demand-side threshold was used.

4 Discussion

Economic analysis of pharmaceuticals is a well-established practice in countries with publicly funded healthcare systems and is often required prior to approval of the new treatments for reimbursement [62]. Economic evaluations are not, however, routinely included in the clinical trials of lifestyle interventions, and many policymakers do not have policies in place to support funding for lifestyle interventions. Policymakers and fund-holders nonetheless have a responsibility to maximize population health within their budgetary constraints. This creates both an opportunity and a problem. On the one hand, lifestyle interventions that support health-related quality of life and rehabilitation of physical function could play an important role in maximising health at both the patient and the societal level. On the other hand, optimal allocation of public funding will require evidence and careful consideration of cost effectiveness across lifestyle, medical, pharmaceutical and other interventions. To assist policymakers in this task, this review summarizes the available evidence, identifies gaps in the evidence base, and discusses implications for optimal allocation of healthcare resources, using Australia as an example, with cost-effectiveness thresholds appropriate for this setting.

Table 5 Cost effectiveness of physical exercise plus concomitant psychosocial counselling on cancer treatment outcomes

Study	Intervention	Cancer type	QALYs gained	Additional costs (AU$)	Incremental net benefit (AUD)		
Braam et al. [48]	24 physical exercise and 6 psychosocial training sessions for the children supplemented by two psycho-educational sessions for the parents	Haematological malignancy	0.030	624	$238	$1763	-$624
Zhang and Fu [31]	Biofeedback pelvic floor muscle exercises plus a support group consisting of 3–5 participants who met biweekly for 3 months	Brain and CNS tumour	0.004	$1485	−$1370	−$1167	−$1485
	Biofeedback pelvic floor muscle exercises plus telephone support. Telephone sessions entailed one-on-one contact with a therapist for 45 min biweekly for 3 months		0.008	$1064	−$834	−$428	−$1064

Evaluating the incremental net benefits of the studies included in this review showed that there was some mixed evidence that lifestyle interventions may be cost effective at the Australian cost-effectiveness threshold when used alongside cancer therapy. Compared with usual care, four of the nine studies reported a positive incremental net benefit value for at least one of the treatment conditions tested (some studies evaluated more than one treatment) and were therefore considered to be cost effective within a constrained healthcare budget (i.e. at the supply-side threshold). If the scenario, however, was one of an expanding budget and a demand-side threshold was applied, then five of the nine studies reported positive INMB values and were considered cost effective. For a scenario where new treatments are only adopted if they impose no additional cost (cost-saving or cost-neutral), then only one treatment was cost effective. Four studies, regardless of the scenario, returned negative INMB values and were therefore not cost effective compared with usual care. These results highlight the importance of the cost-effectiveness threshold and the context in which the cost-effectiveness decision is made.

As the goal of cost-effectiveness analysis is to identify good value, we also need to be confident that the data upon which decisions are made can be relied upon. In their guidance document providing methodology recommendations for health technology appraisal, the UK's NICE (National Institute for Health and Care Excellence) recommends that for ICERs that are greater than £20,000, the degree of certainty around this value should be evaluated [63]. The potential uncertainty arises due to experimental data being generated from samples from within a population and data from a different sample within the population may give rise to a different result. We used 95% confidence intervals to evaluate this stochastic uncertainty, and if the maximum willingness to pay falls within this confidence interval, we cannot be 95% confident that a treatment is good value [33].

Using both the supply-side and demand-side cost-effectiveness threshold we can conclude the interventions used by Retel et al. [53] and May et al. [50] were cost effective, whilst in the setting where new treatments should have no additional cost, only the dominant treatment of May et al. [50] remained cost effective. The sensitivity analysis showed that when the variance was 1.5× larger than that used in the base-case analysis, there was no change in the outcomes. If the variance was overestimated in the base case, then the moderate-high intensity OnTrack exercise intervention of van Waart et al. [51] was additionally considered cost effective.

Ideally, comparison between treatments would be evaluated via meta-analysis. Due to heterogeneity in the included studies (different cancer types, different countries with different healthcare costs, different WTP thresholds, QALYs measured with different instruments, different cost perspectives, and differences in usual care between setting), results could not be pooled to facilitate a meta-analysis.

Guidelines have been published providing recommendations on best practice for conducting and reporting cost effectiveness in economic evaluations [21–23], and these guidelines should be considered by future researchers to standardise economic evaluations. Whilst the methodological quality of the included studies was good overall, there were still flaws in all the studies. One of the most

Table 6 Results of uncertainty and sensitivity analysis. Uncertainty evaluated at the lower limit of the 95% confidence interval. Variance of INMB (incremental net monetary benefit) inflated/deflated to evaluate sensitivity of findings to alternative estimates of sampling error

Study	Intervention	Cancer type	*X*-intercept of LL 95% CI	*X*-intercept lower variance	*X*-intercept higher variance
Braam et al. [48]	Exercises plus psychosocial training	Haematological	Dominated	Dominated	Dominated
Edmunds et al. [49]	Exercise regime	Prostate	Dominated	Dominated	Dominated
Gordon et al. [52]	Exercise regime	Breast	Dominated	Dominated	Dominated
Ha et al. [26]	Exercise regime	Lung	$186,560	$162,730	$229,044
Haines et al. [46]	Exercise regime	Breast	Dominated	Dominated	Dominated
May et al. [50]	Exercise regime	Breast	$1,120,051	$964,017	$1,360,450
		Colon	Dominant	Dominant	Dominant
Retel et al. [25]	Exercise regime	Head and neck	$9622	$8538	$11,460
van Waart et al. [51]	Low intensity exercise	Breast	$231,982	$180,289	$326,282
	Moderate-high intensity exercise		$100,837	$72,836	$149,233
Zhang and Fu [31]	Pelvic floor exercise plus psychosocial support via group counselling	Brain and CNS	Dominant	Dominant	Dominant
	Pelvic floor exercise plus psychosocial support via telephone		Dominant	Dominant	Dominant

Dominated indicates that the *x*-intercept is negative and that INMB is negative at all positive cost-effectiveness threshold values

LL 95% CI lower limit of the 95% confidence interval

important aspects of an economic analysis is ensuring that all relevant costs are considered, and failure to do so may bias the results. The costs that are included, however, depend on the perspective of the analysis. Broadly speaking, the societal perspective is recommended. In this review, five of the nine studies used this (three of the four studies were justified in selection of healthcare perspective). In the remaining study, some relevant costs may not have been included in the analysis. Additionally, travel costs were not included in some studies either due to perspective selected or through omission. In this review, several interventions required frequent travel (e.g. to attend exercise and counselling sessions), and so this omission may impact results.

Most of the reviewed studies evaluated uncertainty through sensitivity analyses. These data provide important information that can help with the evaluation of (i) overall uncertainty regarding estimates of cost effectiveness and (ii) decision-uncertainty associated with the decision to adopt/fund/recommend the evaluated intervention. Whilst most studies reported the use of probabilistic sensitivity analysis using non-parametric bootstrapping, not all included cost-effectiveness acceptability curves and/or scatterplots of the cost-effectiveness plane. These should be routinely included to summarise overall and decision uncertainty and help when transferring the results to different settings.

New treatments are generally evaluated for cost effectiveness in selected countries, and so decision-makers around the world typically need to evaluate whether a new therapy will be cost effective in their setting using results from other countries to inform their decision. The transferability of economic evaluation results is therefore important but has several challenges. Sculpher et al. [43], Welte et al. [44] and Shields and Elvidge [42] identified key barriers to transferability, which include between-study differences in methodology and between-setting differences in the characteristics of both healthcare systems and the population. In this review we adopted an INMB methodological approach that addressed issues of comparability and statistical analysis, and also addressed several transferability factors including differences in currency, inflation, purchasing power and cost-effectiveness thresholds. It is recognised that barriers such as perspective, healthcare system and use, and health-status preference have not been addressed directly, and this is a limitation. Another limitation of this review is that it only considered cost effectiveness in one particular setting (Australia). Funding thresholds differ between countries, as do arrangements for delivery and finance of healthcare, and an intervention that was found to be not cost-effective in the Australian setting may be cost-effective in another setting, and vice versa. Care should therefore be taken when extrapolating these results to different countries and re-evaluation to account for local cost-effectiveness thresholds, inflation and purchasing power may be required. Different cost-effectiveness thresholds were, however, considered to evaluate sensitivity to higher/lower funding thresholds and to increase transferability of our findings.

5 Conclusions

Despite the importance of cost-effectiveness studies for decision making, and even though many patient advocacy groups recommend the use of lifestyle measures to improve outcomes in cancer treatment, there are relatively few cost-effectiveness studies of these interventions in cancer patients. In this review, there is some mixed evidence that may support the use of lifestyle interventions in cancer patients in an Australian setting with four of nine studies returning a positive INMB. However, when uncertainty was accounted for, only two studies were cost effective compared with usual care within the current Australian setting. This review encountered commonly reported issues associated with systematic reviews of cost-effectiveness studies. Although the methodological quality of the included studies was generally good, close adherence to established best practice for cost-effectiveness evaluations is recommended. Whilst the reviewed studies all included data describing the variability of the costs and effectiveness, several of them did not report uncertainty around the ICER. Including measures of dispersion around costs, outcomes and the ICER in study reports (or including covariance between costs and outcomes to facilitate post hoc simulation of ICER) will be beneficial for other researchers. This will help improve comparability and transferability of results and provide better evidence around the cost effectiveness of lifestyle interventions for cancer patients and allowing policy makers to make informed resource allocation decisions.

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Author contributions AG, DM, HT and TH conceived the review, developed the selection criteria, search strategy, risk of bias assessment, data extraction criteria, and analysis plan. AG and VS screened eligible papers, extracted data and conducted risk of bias assessment. AG conducted the analysis and drafted the manuscript. AG, DM, HT and TH reviewed and amended the draft manuscript and approved the final version.

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