SYSTEMATIC REVIEW

Health economic evaluation of weight reduction interventions in individuals suffering from overweight or obesity and a musculoskeletal diagnosis—a systematic review

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Abstract

Background Most of the worldwide population is overweight and suffers from the resulting musculoskeletal comorbidities such as knee osteoarthritis or back pain. Practice guidelines recommend weight loss interventions for individuals suffering from these conditions. This systematic review investigated whether including a weight loss intervention in the musculoskeletal therapy of these individuals was cost-effective compared to administering the musculoskeletal therapy alone.

Methods This study followed the PRISMA guidelines to systematically and independently search six databases and select full health economic evaluations published up to May 2024 from health care or societal perspectives according to predefined eligibility criteria. Cost data were standardised to 2023 Belgium Euros. The methodological quality was assessed using two health economic-specific checklists.

Results The searches produced 5'305 references, of which 8 studies were selected for a total of 1'726 participants. The interventions consisted of different exercise plans and nutritional targets. Six values were in the north-eastern; leading to increased quality-adjusted life year (QALY) and higher costs; and two in the south-eastern quadrant of the cost-utility plane; leading to increased QALYs and lower costs. Two studies observed no differences in QALYs. Incremental cost utility ratios (ICUR) ranged from €13'580.10 to €34'412.40 per additional QALY from a healthcare perspective. From a societal perspective, the ICUR was €30'274.84. The included studies fulfilled 86 percent of the criteria in trial-based economic evaluations and 57 percent in model-based economic evaluations. The most common limitations of the studies were related to appropriate cost measures' specifications, research questions, time horizon choices, and sensitivity analyses.

Conclusions This systematic review showed weak but consistent evidence of cost-effectiveness for adding a weight loss intervention to musculoskeletal therapy for individuals with overweight, from either perspective. Further economic evaluations should evaluate the long-term cost-effectiveness of the intervention.

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Trial registration International Platform of Registered Systematic Review and Meta-analysis Protocols INPLASY (2022,110,122).

Keywords Cost-effectiveness analysis, Health economic evaluation, Weight reduction programs, Weight loss, Overweight, Musculoskeletal diseases

Background

According to the World Health Organization, 58.7 and 23.3 percent of adults older than 18 years in Europe are either overweight or obese [1], respectively. Sex-specific data for Europe indicate that 63.1 percent of men and 54.3 percent of women are overweight [1]. Both conditions are associated with various comorbidities such as type II diabetes, cancer, and cardiovascular diseases [2]. For example, in Belgium, between 2013 and 2017, the healthcare costs for people with a body mass index (BMI) between 25 and 40 kg/m² were 43 and 77 percent higher, respectively, than those for healthy people [3]. In addition, certain musculoskeletal (MSK) disorders, including chronic back pain and osteoarthritis, are common in people suffering from overweight and obesity [2], and numerous studies [4–10] have confirmed the association between low back pain (LBP) and overweight or obese status. People suffering from overweight and obesity seek health care for LBP more often than individuals in the healthy weight category [7]. The total global cost of musculoskeletal disorders related to high BMI worldwide is estimated at \$US180.7 billion [11], which consists of lost productivity costs of \$US 120.2 billion and healthcare costs of \$US 60.5 billion [11].

Based on these statistics, the long-term management of this multimorbid population is essential. A systematic overview of international evidence-based guidelines recommended that the overweight or obese condition should be seen as a chronic disease that requires treatment from a multidisciplinary team of caregivers [12]. A multifactorial, comprehensive weight reduction program that includes reduced calorie intake, increased physical activity and a behavioral change program of a minimum six to twelve months duration is needed to treat individuals with overweight or obesity [12-16]. Similar multimodal lifestyle interventions have been recommended to reduce pain and improve physical function for the treatment of these individuals with MSK diagnoses such as osteoarthritis of the knee [17]. The (cost-)effectiveness of this type of intervention on pain, disability, and quality of life of individuals suffering from overweight or obesity and chronic LBP is unclear [18]. Given the limited resources, the growing number of individuals with these conditions, and the resulting increase in demand for appropriate care, cost-effectiveness studies are essential [19].

To the best of our knowledge, there is currently no literature summary that has analysed, confirmed, or disapproved the cost-effectiveness of non-surgical and non-pharmacological weight reduction programs on pain and physical function in persons with overweight or obesity who have been diagnosed with MSK disorders.

Therefore, this systematic review summarised current full health economic evaluations of weight-loss interventions in the target population using the following specific research question: Are therapies that include weight loss strategies in combination with MSK interventions cost-effective methods of reducing pain and improving function in patients with overweight or obesity and musculoskeletal diagnoses when compared to MSK interventions alone?

Methods

Details of this systematic review were registered on the international platform of registered systematic review and meta-analysis protocols INPLASY (2022,110,122) [20]. This systematic review followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for reporting the research process [21, 22].

Eligibility criteria

Studies were included based on predefined inclusion criteria, which consisted of overweight or obese (i.e., BMI \geq 25 kg/m²) adults aged 18 years and older with an acute or chronic MSK diagnosis. Reports including pregnant or early postnatal mothers were excluded. In addition, studies were required to include the investigation of a weight loss intervention alone or in combination with an MSK diagnosis therapy. Surgical or medical treatments such as medication, alcohol reduction, or smoking cessation for weight reduction were not considered in this systematic review. The comparators used were interventions that only treated the MSK diagnosis and excluded a weight loss program. The primary outcome was the determination of cost-effectiveness (Table 1). Relevant study designs included all trial-based or modelled full health economic evaluations such as cost-effectiveness analyses (CEA), cost-utility analyses (CUA), and cost-benefit analyses (CBA). No restrictions were set regarding sex, country, or language of the study reports.

Page 3	of	18

PICOS elements	Inclusion criteria	Exclusion criteria
Population	Overweight or obese adults (BMI≥25 kg/m²) Age: 18 years and older MSK diagnosis (including chronic conditions)	BMI < 25 kg/m ² Pregnancy Early postnatal mothers
Intervention	Weight reduction therapy—alone or in combination with MSK therapy	Surgical or medical treatment for weight reduction Interventions targeting alcohol reduc- tion and smoking cessation
Comparator	MSK treatment alone	
Outcome	Cost-effectiveness: Incremental cost outcome ratios (ICER, ICUR) Return on Investment (ROI) Benefit–cost ratio (BCR) Net monetary benefit (NMB)	
Study design	Full HEEs: Cost-effectiveness analyses, Cost-utility analyses, Cost–benefit analyses Trial-based HEE (alongside an RCT/ Cohort study) Model-based HEE	Abstracts Congress proceedings Systematic reviews, Meta-analysis Grey literature, Non-academic studies Cost-of-illness study

BCR Benefit-cost ratio, BMI Body mass index, HEE Health economic evaluation, ICER Incremental cost-effectiveness ratio, ICUR Incremental cost-utility ratio, MSK Musculoskeletal, NMB Net monetary benefit, RCT Randomized controlled trial, ROI Return on investment

Abstracts, study protocols, congress proceedings, grey literature, and non-academic studies were not deemed relevant to the analysis. In addition, systematic reviews, meta-analyses, and cost-of-illness studies were excluded. Table 1 summarises the inclusion and exclusion criteria.

Information sources and search strategy

The systematic literature search was conducted in six electronic databases (Medline, Embase, CINAHL, Econlit, Science Citation Index Expanded and Emerging Sources Citation Index, and Scopus). Medline and Embase were accessed through Ovid, while the Science Citation Index Expanded and Emerging Sources Citation Index were retrieved from Web of Science. Predefined and validated search strategies for health economic evaluations were used with all databases [24, 25]. A librarian specialized in search strategy development validated the process, along with some of the co-authors of the present systematic review. The search strategy included search terms for population, intervention, outcome and study design which were combined using Boolean operators. Search terms were only included if they lead to more results in the Medline database. This strategy was then adapted for the other databases. Supplementary file 1 shows the detailed search strategies. The search included studies from inception to May 10th, 2024. Alerts were activated for information from new publications based on the corresponding search strategy for all databases. To ensure that all relevant studies were identified, a forward and backward citation chasing was conducted with the aid of a citation chaser [26].

Study selection

All of the studies identified by the search were independently screened by two researchers (AS, MW), with each researcher reviewing every study for agreement with the inclusion criteria. The title and abstract of each study were screened, and the full text was then analysed and consequently included or excluded. If full texts were not available, the respective authors were contacted. A consensus meeting with a third investigator [12] was held to resolve disagreements in the screening process. Screening was performed using a web application for systematic reviews [27]. The level of agreement of the screening processes was calculated as the ratio of similarly rated studies to the total number of studies screened and presented as a percentage.

Data extraction

Data on the study characteristics and results of health economic evaluations were independently extracted by two researchers (AS, MW) and stored in an a priori developed and tested Microsoft Excel file. These extracted data were compared, and discrepancies were resolved during a consensus meeting with a third reviewer (ML). All intervention characteristics were included in the table of study characteristics for completeness. If a study had e.g. more groups than those relevant to our analysis, these were still included the study characteristics table to ensure comprehensive reporting of all pertinent information from the included studies. If necessary, authors were contacted to receive raw data of the studies.

Data items

Data on the study characteristics (author, publication year, country, and study design), study population (sample size, age, sex, diagnosis, and BMI), and intervention and outcome parameters were extracted. Specific intervention and control group data consisted of sample size, intervention components, duration, number of therapy sessions, and therapy session duration. In addition, the study conclusions were extracted. Outcome-specific data included the health economic evaluation, results summary, study perspective, costs, economic metrics (incremental costeffectiveness ratios (ICER), incremental costs-utility ratios (ICUR), net monetary benefit (NMB), benefit–cost ratio (BCR) and return on investment (ROI)).

Synthesis methods

Quantitative methods for systematic reviews that synthesise results of economic evaluations are difficult to apply due to differences in health care systems worldwide [28]. These vary in aspects such as financing, accessibility, service structure, quality standards, and regulatory practices. Additionally, mathematical issues, such as the pooling of ICER or ICUR, further complicate quantitative synthesis [28]. Therefore, a narrative or qualitative data synthesis is recommended [29]. To increase the comparability of the study results, all available costs of the included studies were converted into 2023 Belgium Euros using the CCEMG EPPI center cost converter with purchasing power parity values (PPP) and the gross domestic product (GDP) deflator index from the International Monetary Fund world economic outlook database [30]. The formula for cost converting is shown below:

$$Cost_{2023 Euros} = \frac{GDP_2 * PPP_2}{GDP_1 * PPP_1} * Cost_{original}$$

The abbreviations stand for:

 GDP_1 is the GDP deflator index for the study currency in the referenced price year;

 GDP_2 is the GDP deflator index for the study currency in the price year 2023;

 PPP_1 is the PPP conversion rate for the study currency in the price year 2023;

 PPP_2 is the PPP conversion rate for the target currency (euros) in the price year 2023 and.

Cost_{original} is the price in the study currency in the original currency [30].

The health economic metrics considered were recalculated based on the value of the Belgium Euro for 2023. The calculated cost and quality of life values (including reported confidence intervals) were then plotted in a cost-effectiveness or cost-utility plane to visualise the cost-effectiveness. The CEA of an intervention or stakeholder group can be quantified using the ICER and ICUR.

Both measures (ICER and ICUR) are used in health economics to assess the value of an intervention compared to an alternative. The costs associated with each study group are considered, depending on the perspective of the analysis. For the ICER, a clinical outcome parameter is used to evaluate effectiveness. For the ICUR, utilities derived from a quality of life questionnaire, typically measured in Quality-Adjusted Life Years (QALYs), are used to capture the intervention's impact on both the quantity and quality of life. ICER and ICUR are calculated as follows: These are calculated as follows:

 $\text{ICER or ICUR} = \frac{\textit{Costs}_{\textit{Weightloss Intervention}} - \textit{Costs}_{\textit{Control Intervention}}}{\textit{Effects}_{\textit{Weightloss Intervention}} - \textit{Effects}_{\textit{Control Intervention}}}$

Depending on availability in the included studies, ICER and ICUR values were available if one intervention was not already evaluated as being dominant in the cost-effectiveness plane. This is, for example, the case in therapies that are cheaper compared to the control intervention but lead to similar or better effects. Calculation of the ICER or ICUR was also omitted in the included studies if no additional clinical effects were achieved by the therapy. This would otherwise lead to extremely high ICER and ICUR values.

The CBA metrics used were ROI, BCR and NMB [31]. The following measures were used for the cost–benefit analysis:

$$ROI = \frac{(Benefits - Investment)}{Investment} * 100\%$$

$$BCR = \frac{Benefits}{Investment}$$

The cost-benefit analysis was conducted based solely on the costs, without monetising the effects, to avoid double counting [23, 32, 33]. Productivity costs do account for the effects of changes in quality of life. Including clinical effects in the cost-benefit analysis would result in double counting these outcomes. Positive values for ROI and NMB indicate that the option is cost-beneficial [31], along with a BCR of greater than one [31, 34].

The subgroup analyses were conducted based on the type of the control group, whereby the combined weight loss with MSK therapy group was compared to an exercise-based intervention alone or a non-exercise-based control intervention. Separate planes were utilised for each perspective, resulting in two planes per subgroup analysis. The health-care perspective focuses only on direct medical costs, whereas the societal perspective encompasses all costs, including both direct and indirect costs [35].

Methodological quality appraisal

The methodological quality of the studies was assessed based on the study design. Health economic evaluations that considered randomised controlled trials were assessed using the Consensus Health Economic Criteria (CHEC) list [36], which is a generally accepted list of 19 yes-or-no questions. A "yes" response indicates that the study paid sufficient attention to the aspect in question, while a "no" response is recorded if insufficient information was available. If a criterion did not apply to the study, it was marked as "not applicable".

To evaluate the potential risk of biases more specifically for model-based health economic evaluations, these studies were assessed using the Bias in Economic Evaluation (ECOBIAS) checklist [37]. It assesses biases using five options: "yes", "no", "partly", "unclear", or "not applicable". Two assessors (AS, MW) independently performed the assessments and a consensus meeting with a third researcher (ML) was organized in cases of discrepancy. The agreement levels for the methodological quality ratings from both reviewers were described in percentages.

Results

Study selection

Figure 1 depicts the PRISMA flowchart used to identify relevant studies for this systematic review. The literature search yielded 4'925 references including 1'134 duplicates. A total of 380 studies were found using the citation chasing. Full-text screening of 14 studies was conducted.

The most common exclusion criteria related to the intervention (n=2), population (n=2), study design (n=1), and outcome (n=1). Although the study by Kostic et al. [38] appeared to meet the inclusion criteria, it was excluded during the full-text screening due to the potential use of a weight loss medication (Orlistat) in the intervention group. Eight reports were included in the systematic review. The level of agreement for the two screening stages of the two reviewers (AS, MW) were 99 and 90 percent, respectively (Fig. 1).

Study characteristics

Six of eight included reports were characterised as health economic evaluations alongside randomised controlled trials [39–44], whereas two studies were model-based evaluations [45, 46]. No CBAs were included. Seven studies were CUA [39–42, 44–46], and

three of these included a CEA [41, 42, 44]. One study performed a CEA [43] only. The studies were conducted in Australia (n = 3), the United States (n = 3), the United Kingdom (n = 1), and the Netherlands (n = 1). Time horizons included studies of up to one year [40–42, 44] or greater than one year [39, 43, 45, 46], ranging from 26 [40] to 109 weeks [39].

The eight included studies assessed 1'726 participants, of whom 41 percent were men and 59 percent were women. The two model-based studies did not report any numbers of participants. All investigated groups were included in the total participation calculation, whereas only the subgroups meeting all inclusion criteria were considered for the analysis. The included studies investigated individuals who were overweight or obese and experienced either self-reported knee pain [39], knee osteoarthritis [39, 41–43, 45, 46] or chronic low back pain [44]. The BMIs ranged between 27 and 40 kg/m². Table 2 details the general characteristics of the studies.

Interventions

The treatments among most of the studies were heterogenous. Two studies used on-site treatment [39, 41], three provided online [40] or telephone-based therapy [42, 44], and one used a hybrid treatment delivery combining onsite with telephone-based treatment [43]. The studies by Losina et al. and Kopp et al. did not specify the content of the intervention therapy [45, 46]. Different dietary goals were set for the interventions. One study utilised a personalized diet plan developed by a dietitian that targeted a caloric restriction of 600 kilocalories per day [39], and three studies set targets of five or ten percent overall weight loss until the end of the intervention [40-42]. Harris et al. chose a ketogenic, low-calorie diet, whereas the other studies did not specify the dietary intervention. Only three studies specified the type of exercise training. Barton et al. [39] included a quadriceps muscle strengthening program along with other exercises using different resistance bands, Sevick et al. [43] combined aerobic training at a 50 to 85 percent heart rate reserve with resistance training, while Knoop et al. [41] integrated an obesity-adapted supervised exercise therapy aimed at strengthening thigh muscles, increasing aerobic capacity, and enhancing weight loss in combination with an educational component.

The control interventions, either added to the weight reduction program or delivered in the control group alone, included different MSK interventions. These varied from quadriceps muscle therapy alone [39], combined aerobic and resistance training [43], leaflet provision and educational support at home for exercise training at home [40], non-steroidal drug administration, and knee arthroplasty [45, 46]. One study described the control

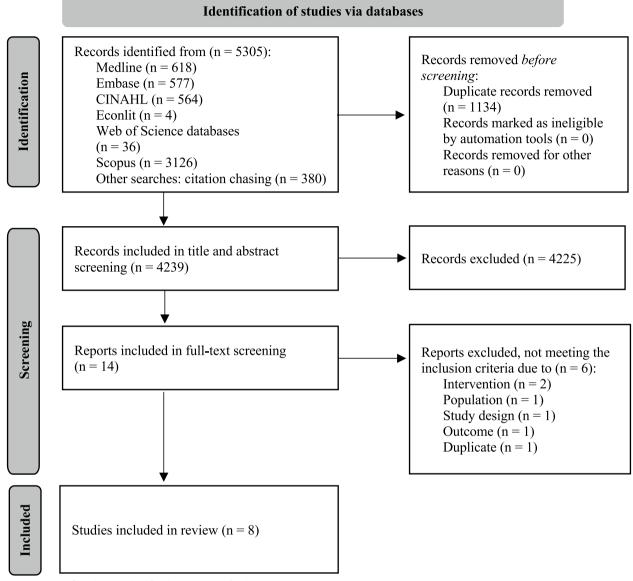


Fig. 1 PRISMA flowchart to identify relevant studies for the systematic review

intervention as normal care according to the physical therapy guidelines [41], which consisted of exercise therapy accompanied by patient education [41]. Two studies compared the intervention to the standard care pathway that constituted waiting for an orthopedic consultation [42, 44].

Effects

Different questionnaires on quality of life (EQ-5D, Aqol-8D, SF-6D) [39–42, 44] were used to report the effects of the treatments. While the studies by Losina et al. and Kopp et al. did not specify the data collection method, Sevick et al. did not report their data

quantitatively [43, 45, 46]. All studies except for the of O'Brien et al. [42], Knoop et al. [41] and Barton et al. [39] studies showed that the interventions had greater effects on the patients than the control treatments. These three studies had lower 95 percent confidence intervals below 0. Incremental mean effect values ranged from 0.020 to 0.062 for all quality-of-life questionnaires. (Table 3). Values on the numeric rating scale (NRS) of pain intensity (knee or low back pain) did not differ in the intervention group compared to the control group in the two studies [42, 44]. In the Sevick et al. study, the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) was

Study	Aim	Participants	Intervention	Control condition	Outcome	Author´s conclusion
Barton et al., 2009, [39] UK: CUA alongside RCT: 109 wk	To investigate cost-effec- tiveness of interventions for knee pain	n = 389 Age: mean: 61.3 y; 132/257 (34%/66%); self-reported knee pain, overweight, obesity; BMI:≥ 28 kg/m ²	<i>n</i> = 109: Content: Dietary interven- tion plus quadriceps strengthening exercise (104 wk, mean 11.19 ses- sions, <i>/</i>)	<i>n</i> =82: Content: Quadriceps strengthening exercises (104 wk, mean 4.95, /) <i>n</i> = 76; leaflet provision (104 wk, mean 6.05, /) <i>n</i> = 122; dietary intervention (104 wk, //)	Primary outcomes: EQ-5D	Dietary intervention plus strengthening exer- cises was estimated to be cost-effective for individuals with knee pain
Harris et al., 2022, [40] AUS: CUA alongside RCT: 26 wk	To estimate the 12-month cost-effectiveness of telehealth-delivered programs	<i>n</i> = 415 Age: range: 45–80 y; Sex: 187/227 (45%/55%); KOA, overweight, obesity; BMI: 28–40 kg/m ²	n = 175 Content: Diet plus exercise program: (26 wk, 6, /)	 n=172; Content: Exercise program for home exercise, physical activity plan, self-manage- ment advice, behavioral counselling plus exercise equipment, printed resources: (26 wk, /, /) n=67; educational control (26 wk, /, /) 	Primary outcome: AQol-8D	A telehealth-delivered program targeting exercise, WL and self-management for people with KOA who have overweight/obesity had a high probability of being cost-effective compared to online infor- mation within 12 months and compared to an exer- cise only program
Knoop et al., 2023, [41] NDL: CEA/CUA alongside RCT: 52 wk	To evaluate the cost-effectiveness of stratified exercise therapy compared to usual exercise therapy, from the societal and healthcare perspectives	<i>n</i> = 328 Age: range: 40–85 y, mean: 1: 66y, C: 64y; Sex: 119/209 (36%/64%); KOA, subgroup with obe- sity; sity; C: 28.6 kg/m ² , C: 28.6 kg/m ² ,	n = 34 Content: Education, supervised exercise therapy for upper leg muscle strength, aerobic capacity, weight loss, capacity, weight loss, home exercises, dietary intervention (52 wk, 12-18 exercise, 2–3 boster, 5–8 dietary, dietary max 150 min)	n=53 Content: Usual care (exer- cise, education) (52 wk, 12, /)	Primary outcomes: EQ-5D-5L, average knee pain severity while walk- ing in past week (NRS 0–10)	No clear evidence that stratified exercise therapy is likely to be a cost- effective option compared to usual exercise therapy in patients with KOA

 Table 2
 General study characteristics of the studies included in the systematic review

Study	Aim	Participants	Intervention	Control condition	Outcome	Author's conclusion
Kopp et al., 2024, [41] US: Model based HEE: up to 78 wk, lifetime evaluation	To establish the value of diet and exercise and health education programs to facilitate their implementation into regular knee OA care	n=/ Age: mean: 64.6 y; Sex: / (23%/77%); KOA, overweight, obesity; BMI> 27 kg/m ²	n=/ Content: Diet and Exer- cise: Usual care + group nutrition classes, exercise classes, meal replacement shakes	n=/ Content: Usual care: NSAID or other analgesics, corticosteroid injec- tions, opioids, total knee arthroplasty, revision arthroplasty n=/ Content: Health educa- tion: Usual care + group classes to improve knowl- cdge related to nutrition and healthy lifestyle	Primary outcome: QALY	Our OAPol model-based cost-effectiveness analysis found that D+E could be cost-effective when added to UC clinical management for patients with over- weight or obesity and knee OA for decision makers will- ing to pay up to \$62,000/ QALY
Losina et al., 2019, [46] US. Model based HEE: up to 104 wk	To evaluate the long-term cost-effectiveness of com- bining a diet & exercise regimen to usual care	n =/ Age: mean: 66 y; Sex: / (28%/72%) KOA, overweight, obesity; BMI: 28–40 kg/m ²	n=/ Content: Diet plus exercise program: (up to 104 wk,/,/)	n=/ Content: NSAID, total knee arthroplasty, revision total knee arthroplasty: (up to 20 years, annual visit, /)	Primary outcome: QALY	Our analysis suggests that incorporating a diet and exercise regimen into usual care treat- ment for KOA would be highly cost-effective from both societal and healthcare sector perspectives
O Brien et al., 2018, [42] AUS: CUA/CEA alongside RCT: 26 wk	To undertake an eco- nomic evaluation of the RCT, compared to usual care	n = 119 Age: mean: !: 63.0 y, C: 60.2 y; Sex: 45/74 (38%/62%) KOA, overweight, obesity: BMI: mean: : 33.1 kg/m ² , C: 32.1 kg/m ² , Tange: 27-40 kg/m ²	n = 59 Content: WL support from Get Healthy Informa- tion and coaching service, advice, education, activity (telephone based): (26 wk, mean: 4.7, /)	n=60 Content: Usual care path- way (Waiting list for ortho- pedic consultation): (26 wk, 0, /)	Primary outcome: SF-6D, average knee pain intensity (NRS 0–10)	Our findings suggest that referral to a telephone- based weight manage- ment and healthy lifestyle service is not cost-effective compared to usual care for patients with over- weight or obesity and KOA
Sevick et al., 2009, [43] US: CEA alongside RCT: 78 wk	To compare the cost- effectiveness of diet and exercise interventions	n = 316 Age: mean: 69 y; Sex: 66/168 (28%/72%) KOA, overweight, obesity: BMI: mean: I: 34.2, C: 34.2 & 34.0	n = 76 Content: Diet and Exercise: (78wk, 234, 60 min)	 n=80 Content: Exercise alone: aerobic, resistance: (78 wk, /, /) n=78 Content: Healthy lifestyle control: videos, physician talks on osteoarthritis, exercise, dietary weight loss, phone calls (12 wk, 3, 60 min) n=82 Diet (78 wk, 16, /) 	Primary outcome: WOMAC	The exercise and diet intervention were usually the most cost-effective approach to improv- ing clinically meaningful outcomes of self-reported physical function, pain and stiffness

Study	Aim	Participants	Intervention	Control condition	Outcome	Author's conclusion
Williams et al., 2019, [44] To undertake an eco- AUS: CEA/CUA alongside nomic evaluation RCT: 26 wk of the healthy lifestyle intervention, compare with usual care	To undertake an eco- nomic evaluation of the healthy lifestyle intervention, compared with usual care	n = 159 Age: mean: 1: 56.0 y, 5.7.4 y Sex 65/94 (40%/60%) Chronic low back pain, overweight, obesity: BMI: mean: 1: 32.4 kg/m ² , C: 32.1 kg/m ² , range: $\geq 27 < 40$ kg/m ²	n = 79 Content: Brief telephone advice, clinical consulta- tion with physiothera- pist, referral to 6 month telephone-based health coaching service: (26 wk, 10, 60 min)	n=80 Primary outcome: SF Content: Remained average low back pa on waiting list for orthope-intensity (NRS 0–10) dic consultation: (26 wk, 0, /)	Primary outcome: SF-6D, average low back pain intensity (NRS 0–10)	Intervention was on aver- age less expensive and more effec- tive than usual care from societal perspective and was associated with rel- atively high probabilities of being cost-effective compared to usual care
Participants: Sex: male/femal	Participants: Sex: male/female (male%/female%); Intervention/control group: number of participants, components (duration, number of sessions, duration of one session)	on/control group: number of pa	rticipants, components (duratic	Participants: Sex: male/female (male%/female%); Intervention/control group: number of participants, components (duration, number of sessions, duration of one session)	of one session)	

Table 2 (continued)

Abbreviations: AQoI-BD Assessment of quality of life-8 dimensions, AUS Australia, BMI Body mass index, C Control group, CEA Cost-effectiveness analysis, CUA Cost-utility analysis, EQ-5D EuroQol questionnaire-5 dimensions, I Intervention group, KOA Knee osteoarthritis, min minutes, NDL Netherlands, NRS Numeric rating scale, NSAID Non-steroidal anti-inflammatory drugs, SF-6D 12-item Short Form Health Survey, QALY Quality-adjust life year, RCT Randomised Controlled Trial, UK United Kingdom, US United States, wk weeks, WL Weight loss intervention, WOMAC Western Ontario and McMaster Universities osteoarthritis index, y years

Table 3 Effects and costs of included studies

Study	Incremental ef	fect	Incremental cos	ts (converted to 20	023 Belgium Euro	os)	
	Quality of Life	Clinical parameter	Intervention costs	Mean direct medical costs	Mean direct non-medical costs	Mean indirect costs	Mean total costs
Weight loss interv	vention versus ex	ercise					
Harris et al., 2022 [40]	<i>Aqol-8D:</i> 0.02 (0.01; 0.04)	n.a	n.r	1,130.80 (1,076.40; 1,178.73)	n.r	n.r	h: 285.62* (-645.71; 1140.52)
Knoop et al., 2023 [41]	<i>EQ-5D</i> : 0.01 (-0.01; 0.04)	n.a	89.62 (n.r.; n.r.)	601.27 ^a (-1,281.63; 2,492.70)	n.r	n.r	h: 601.27 (114.41; 1,088.12) s: -266.7 (-2,753.26; 2,262.18)
Sevick et al., 2009 [43]	n.r	n.a	3,680.27 (n.r.; n.r.)	64.28 (n.r.; n.r.)	n.r	n.r	h: 3,744.55* (n.r.; n.r.)
Weight loss interv	ention versus no	n-exercise control					
Barton et al., 2009 [39]	<i>EQ-5D</i> : 0.06 (-0.04; 0.17)	n.a	n.r	n.r	n.r	n.r	h: 1,131.96 (1,011.96; 1,242.08)
<i>Harris</i> et al., 2022 [40]	<i>Aqol-8D</i> : 0.05 (0.03; 0.07)	n.a	1,501.91 (n.r.; n.r.)	1,501.26 (1,456.57; 1,545.95)	n.r	n.r	h: 1,422.25* (450.77; 2,369.77)
<i>Kopp</i> et al. <i>2024</i> [41]	n.r: 0.13 (n.r.; n.r.)	n.a	5,459.98 (n.r.; n.r.) (n.a.; n.a.)	n.r	n.r	n.r	n.r
<i>Losina</i> et al., 2019 [46]	n.a.: 0.05 (n.r.; n.r.)	n.a	n.r	n.r. ^b	n.r	n.r	h: 1,861.90 (n.r.; n.r.) s: 1,638.88 (n.a.; n.a.)
O'Brien et al., 2018 [42]	SF-6D: 0.00 (-0.02; 0.02)	Pain intensity NRS: 0.64 (-0.49; 1.77)	443.73 (338.15; 562.15)	351.70 (-2,506.14; 3,825.91)	n.r	89.17 (107.72; 346.71)	h: -764.04 (-4,216.14; 2,090.95) s: 853.93* (-2,059.56; 4,355.96)
Sevick et al., 2009 [43]	n.r	n.a	6,620.66 (n.r.; n.r.)	80.69 (n.r.; n.r.)	n.r	n.r	h: 6,701.35 (n.r.; n.r.)
<i>Williams</i> et al., 2019 [44]	<i>SF-6D</i> : 0.02 (0.00; 0.04)	Pain intensity NRS: -0.35 (-1.33; 0.64)	505.08 (414.48; 606.38)	-208.31 (-622.08; -23.54)	n.r	-713.39 (-2,548.94; -149.81)	h: 275.37 -134.12; -490.81) s: -438.02 -2,235.05; 181.91)

Values are means (95% Confidence intervals), rounded to 2 decimal places

Abbreviations: Agol-8D Assessment of Quality of Life—8 dimensions questionnaire, EQ-5D EuroQol 5 levels Quality of Life questionnaire, h ca care perspective, m months, n.a. data not applicable, n.r.: data not reported, NRS Numeric Rating Scale, s societal perspective, SF-6D Short Form- 6 dimensions Health Index, WL Weight loss

*: adjusted values

^a Direct medical costs included other medical costs which included primary health care costs other than the intervention (e.g. hospital, rehabilitation center), secondary health care (e.g. hospital, rehabilitation center) and prescribed and over-the-counter medication for knee osteoarthritis only

^b Incremental mean direct medical and total costs could not be calculated as the control group received non-steroidal anti-inflammatory drugs, a primary total knee arthroplasty and possibly a revision total knee arthroplasty

^c Costs were adjusted for this value for confounders of baseline knee pain intensity, baseline duration of knee pain, baseline body mass index, number of days on the waiting list for orthopaedic consultation

reduced significantly more in the intervention group compared to the control group; these values were only reported in text form without stating specific values in the latter study [43] (Table 3).

Costs

Table 3 shows the relevant cost data. Barton et al. [39] performed the only study that reported aggregated cost-related data. The modelled studies by Losina et al.

and Kopp et al. did not report any confidence intervals of the cost values and only specified the costs for total costs [45, 46].

Incremental intervention costs were reported in five studies [40-45], ranging from 89.62 Euros to 6,620.66 Euros (2023 Belgium Euros). Mean direct medical costs were reported in five studies [40-44] with these costs ranging from -208.31 Euros to 1,130.80 Euros (2023 Belgium Euros). Incremental direct non-medical costs were not reported in any study, while indirect costs were reported in two studies [42, 44]. Incremental indirect costs in these two studies were 89.17 Euros [42] and -713.39 Euros [44]. The studies by Harris, Losina and Williams reported increased incremental total costs ranging from 275.37 Euros to 1,861.90 Euros from a healthcare perspective and for the Williams study -438.02 Euros from a societal perspective [40, 44, 46]. The other studies did not indicate a consistent trend towards increasing or decreasing total cost differences, regardless of perspective.

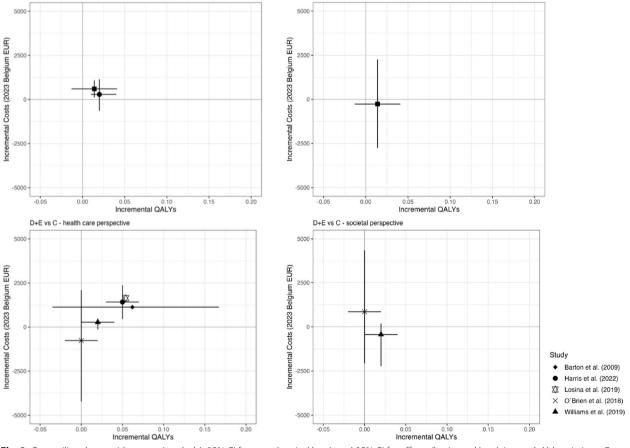
D+E vs E - health care perspective

When analysing the cost-utility values, ICURs from six of the seven studies conducted from the healthcare perspective were situated in the north-eastern quadrant of the cost-effectiveness plane (Fig. 2); indicating higher costs alongside increased QALYs; and from the societal perspective, two of three studies in the south-eastern quadrant of the plane; indicating lower costs with increased QALYs (Fig. 2).

O'Brien et al. did not show additional clinical effects and was therefore positioned on the y-axis of the costeffectiveness plane [42]. Kopp et al. could not be reported in the plane due to missing incremental total cost values [45] (Table 4).

Sevick et al. reported \notin 32.82, \notin 27.35 and \notin 76.59 per percentage improvement in the WOMAC subcategories of function, pain, and stiffness [43].

Data in the cost-effectiveness plane referring to knee or back pain intensity, were found in all four quadrants of the cost-effectiveness plane [42, 44] (Fig. 3).



D+E vs E - societal perspective

Fig. 2 Cost-utility planes with means (symbols), 95% CI for costs (vertical bars), and 95% CI for effects (horizontal bars). Legend: Abbreviations: C: Non-exercise control group; D + E: Diet and exercise therapy; E: Exercise therapy; QALYs: Quality-adjusted life years

Table 4 Ov	verview of resu	Table 4 Overview of results of included studies. Costs	studies. Costs	adjusted to 2(adjusted to 2023 Belgium Euros	uros						
Study	Perspective	Reference	Discount	Threshold		Incremental	Incremental	Return on	Benefit-	Net	Sensitivity analysis	alysis
		value in original study	Late	in orginal study	Average incremental cost per average incremental gain	cost- effectiveness ratio (ICER)	cost-utility ratio (ICUR)	(ROI)	(BCR)	monetary benefit (NMB)	Was a sensitivity analysis conducted? If yes, which method?	Were the results robust?
Weight loss	Weight loss intervention versus exercise	rsus exercise										
Harris et al., 2022 [40]	Health sector 2020 Austral- ian Dollars	2020 Austral- ian Dollars	n.a	\$AUS 70 k/ QALY	n.a	n.a	h: €13,665.50 per QALY	n.r	n.r	n.r	Yes, Unclear	Yes
Knoop et al., 2023 [41]	Health sec- tor, Societal	2020 Nether- lands Euro	е́ц	ENDL 0-50 k/ QALY	n.a	s: dominated	s: dominated	h: 571% (28%; 1,114%) s: -398% (-3172%; 2,424%)	h: 6.71 (1.28, 12.14) 5: -2.98 (-30.72; 25.24)	h: 511.65 (24.79; 998.50) s: -356.32 (-2,482.88; (-2,482.88; 2,172.56)	Yes, different ways; e.g. human capi- tal approach, stratified per sub- group	Yes
Sevick et al., 2009 [43]	Health sector	Health sector 2000 US Dol- lars	5%	e C	WOMAC function: 32.826/ % improve- ment pain: 627.35/ pain: 627.35/ % improve- % improve- ment	n.ar	J.	h: 2% (n.r.; n.r.)	h: 1.02 (n.r.; n.r.)	h: 64.28 (n.a.; n.r)	Yes, One-way	Yes
Weight loss	Weight loss intervention versus control	rsus control										
Barton et al., 2009 [39]		Health sector 2006/2007 UK sterling £	3.5%	20-30 k £/ QALY	n.a	n.a	h: €18,639.41 per QALY	n.r	n.r	n.r	Yes, Unclear	Yes
Harris et al., 2022 [40]	Health sector		n.a	\$AUS 70 k/ QALY	n.a	вл	h: €29,468.27 per QALY	h: -5% (-70%; 58%)	h: 0.95 (0.30; 1.58)	h: -79.66 (-1,051.14; 867.86)	Yes, Unclear	Yes
Kopp et al., 2024 [41]	Health sec- tor, Societal	2020 US Dol- lars	n.a	n.a	n.a	'na	h: €59,363.9 per QALY s: €57,863.39	n.r	n.r	n.r	Yes, One-way and two-way (determinis- tic, probabil- istic)	Yes

Incremental cost-utility ratio (ICUR) Return on ROU Benefit- cost-ratio (BCR) Net benefit Sensitivity analysis conducted? intio (ICUR) (ROU) (BCR) Net cost-utility investment Net cost-ratio (BCR) Sensitivity analysis conducted? intio (ICUR) (ROU) (BCR) Net cost-utility investment Net cost-utility is conducted? Sensitivity analysis conducted? intio (ICUR) nr nr nr nr Yes, on-way per QALY per QALY hr172 hr172 hr1,20777 Yes, on-way per QALY per QALY conducted? 1,347% it; probabil- it; probabil- it; probabil- it; Yes, on-way per QALY na hr172 hr1,20777 Yes, no addi- culated Yes, on-way per QALY na hr.196 hr.101 n. Yes, on-way per QALY na hr.196 hr.101 hr.80.69 Yes, One-way per QALY na hr.196 hr.101 hr.80.69 Yes, Unclear per QALY se dominant effect, ICER hr.101 hr.80.69 Yes, Unclear per QALY na hr.198 e.087 s043.10 se dominant effect, ICER hr.22971 Yes, Unclear per QALY na hr.198 e.032 e.943.10	lable 4 (continued)												
Value in original study original study rest study incremental	Study	Perspective	Reference	Discount	Threshold		Incremental	Incremental	Return on	Benefit-	Net	Sensitivity ar	alysis
V Health sec. 2016 US Dol- 3% SUS 50 k/ OALY na h: E34,412.40 per QALY nr nr rr Yes, One-way (deremnis- se: 30,27484 tor, Societal lars SUS 500 k/ SUS 200 k/ OALY OALY per QALY per QALY tr Tr Yes, One-way (deremnis- ser, 2016 Austral- L, Health sec- 2016 Austral- na Na SUS 200 k/ OALY na kree pain not h: -172 irt, probabi- st(c) L, Health sec- 2016 Austral- na SUS 200 k/ OALY na kree pain not h: -172 irt, probabi- st(c) L, Health sec- 2016 Austral- na SUS 200 k/ OALY na na h: -172 irt, n120777 Yes, One-way (c) L, Health sec 2016 Austral- na na na h: -172 irt, n120777 Yes, One-way (c) L, Health sec 2016 Austral- na na h: -172 irt, n120777 Yes, One-way (nr; nn) L Health sector 2000 US Dol- 5% na na h: 19% h: 101 h: 8069 Yes, One-way (nr; nn) L Health sector 2000 US Dol- 5% na na h: 19% h: 101 h: 8069 Yes, Uncear (nr; nn) Health sec			value in original study	Tate	in original study	Average incremental cost per average incremental gain	cost- effectiveness ratio (ICER)	cost-utility ratio (ICUR)	Investment (ROI)	(BCR) (BCR)	monetary benefit (NMB)	Was a sensitivity analysis conducted? If yes, which method?	Were the results robust?
I, Health sec- tor, Societal an Dollars an Dollars sAUS 0/QALY n.a knee pain intensity: brint decrease on NRS (SE) not filteral second second second second ans h:-172 (4,554,25) (4,554,25) h:-1,272,312 (4,554,25) h:-1,272,312 (4,554,25) h:-1,272,312 (4,554,25) h:-1,272,312 (4,554,25) h:-1,272,312 (4,554,25) h:-1,272,312 (4,528,00) Per-protocol (4,534,25) Per-protocol (4,534,25) A Health sector 2000 US Dol- lars 5% n.a n.a n.a n.a n.a h:1,101 h:8069 Yes, One-way (n.c,n.l) Health sector 2000 US Dol- lars 5% n.a n.a n.a n.a h:1,101 h:8069 Yes, One-way (n.c,n.l) Health sector 2016 Austral- n.a n.a n.a n.a h:e13,58010 h:e13,58010 h:e3,59030 Yes, Unclear Health sec- lars 2016 Austral- n.a n.a n.a n.a h:e13,58010 h:e13,680 Yes, Unclear Kot, Societal an Dollars 2016 Austral- n.a h:e13,58010 h:e13,58010 h:e13,680 Yes, Unclear Kot, Soci	Losina et al., 2019 [46]	Health sec- tor, Societal	2016 US Dol- lars	3%	\$US 50 k/ QALY \$US 100 k/ QALY \$US 200 k/ QALY	n.a	n,à	h: €34,412,40 per QALY s: €30,274,84 per QALY	že	Ĵ.	ĩ	Yes, One-way (determinis- tic, probabil- istic)	Yes
Health sector 2000 US Dol- 5% n.a n.a n.a n.a in 1.01 h: 80.69 Yes, One-way Iars iars n.a n.a n.a n.a in 1.01 h: 80.69 Yes, One-way Health sec- 2016 Austral- n.a back pain h: e13.580.10 h: 45% h: 0.55 H: -229.71 Yes, Unclear Health sec- 2016 Austral- n.a 5AUS 0/OALY n.a back pain h: e13.580.10 h: 475% h: 0.55 H: -229.71 Yes, Unclear tor, Societal ian Dollars SAUS 17 kL intensity: per OALY (-132% (0.32; (-548.60; OALY SAUS h: 6733.51/ s: dominated -181% 0.811 -1.097.19 -0.097.19 67 k/OALY on NRS (NW) (-639%; (-539; 0.30) (-549.53; s: -943.10 for torist s: -1.259.13 7/0% s: -187% s: -943.10 -424.47 for non NRS (SW) c.639%; (-5.39; 0.30) (-249.53; -424.47 -424.47	O'Brien et al., 2018 [42]		2016 Austral- ian Dollars	ē.	\$AUS 0/QALY		knee pain intensity: h: €883.18/ point decrease on NRS (SE) s: €1,325.48 per point decrease on NRS (NE)	not dominant, no addi- tive clinical effect, ICER was not cal- culated	h: -272% (-1,347%; 272%) s: 92% (-709%, 675%)	3.72) 75)	h: -1,207.77 (-4,554.29; 1,528.80) 5:410.20 (-2,397.71; 3,793.81)	Yes, Per-protocol	Yes
Health sec- 2016 Austral- n.a \$AUS 0/OALY n.a back pain h.: 45% h.: 0.55 H.: -22971 Yes, Unclear tor, Societal ian Dollars \$AUS 17 k/ intensity: per QALY (-132%); (-0.32; (-548.60; QALY \$AUS h.: €733.51/ s: dominated -181%) -0.81) -1,097.19) 67 k/QALY point decrease s: -187% s: -0.87 s: -943.10 67 k/QALY point decrease s: -187% s: -0.87 s: -943.10 67 k/QALY point decrease s: -187% s: -0.87 s: -943.10 67 k/QALY point decrease s: -187% s: -0.87 s: -943.10 67 k/QALY point decrease s: -187% s: -0.87 s: -943.10 67 k/QALY point decrease s: -187% (-5.39; 0.30) (-2649.53; 67 k/QALY point decrease s: -187% s: -9.37 -424.47)	Sevick et al., 2009 [43]	Health sector		5%	n.a	n.a	n.a	n.a	h: 1% (n.r.; n.r.)	h: 1.01 (n.r.; n.r.)	h: 80.69	Yes, One-way	Yes
	Williams et al., 2019 [44]	Health sec- tor, Societal	2016 Austral- ian Dollars	Р. Ц	\$AUS 0/QALY \$AUS 17 K QALY \$AUS 67 K/QALY		back pain intensity: h: €733.51/ point decrease on NRS (NW) s: €-1,259.13 per point decrease on NRS (SW)	h: €13,580.10 per QALY s: dominated	h: -45% (-132%; -181%) s: -187% (-639%; -70%)	h: 0.55 (-0.32; -0.81) s: -0.87 (-5.39; 0.30)	H: -229,71 (-548,60; -1,097,19) 5: -943,10 (-2649,53; -424,47)	Yes, Unclear	° N

Abbreviations: AUS Australia, C Control, D+E Diet and Exercise therapy, E Exercise, h Health care perspective, k Thousand, n.a. not applicable (duration of study < 1 year), n.r. not reported, NE North-eastern quadrant of cost-effectiveness plane, QALY Quality-adjusted life years, s societal perspective, 5E South-eastern quadrant of cost-effectiveness plane, SW South-western quadrant of cost-effectiveness plane, J y South-western quadrant of cost-effectiveness plane, SW South-western quadrant of cost-effectiveness plane, J y south-western q * adjusted values

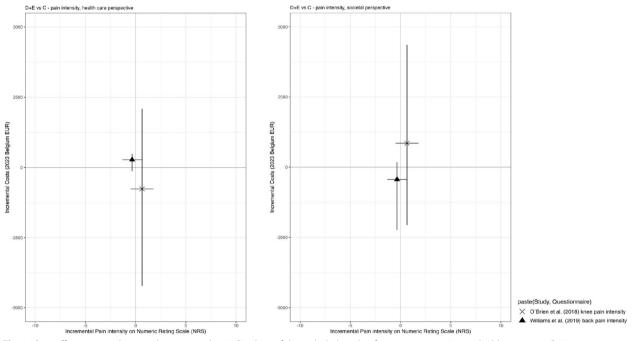


Fig. 3 Cost-effectiveness planes with means and 95% CI values of the included studies for pain intensity. Legend: Abbreviations: C: Non-exercise control group; D + E: Diet and exercise therapy; E: exercise therapy

Cost-benefit analyses

Table 4 shows the results of CBA. CBA could not be performed for the Barton et al., Kopp et al. and Losina et al. studies [39, 45, 46]. The cost-benefit analyses which compared diet and exercise interventions with an exercise control group, led to ROI values above the threshold of 1 from a health care perspective [41, 43]. When comparing the weight loss program with a non-exercise control group, the ROI, NMB, and BCR values in total five studies had contrasting results from both the societal and health care perspectives [40, 42–44] (Table 4). Mean ROI values ranged from -272 percent [42] to 571 percent [41], while mean BCR values ranged from -1.72 [42] to 6.71 [41] and NMB values from -1,207.77 [42] to 511.65 [41].

Methodological quality appraisal

Six studies were evaluated using the CHEC list [39–44]. The two model-based health economic evaluation studies were assessed for methodological quality using the ECOBIAS criteria [45, 46]. The overall quality of the eight studies were moderately strong including some methodological gaps. Eighty-six per cent of the criteria received "yes" ratings in the CHEC list, eleven were assessed as "no" or "not applicable". Fifty-seven per cent of the ECO-BIAS criteria were included in the evaluated studies, with sixteen per cent absent or seven per cent partly included, and twenty per cent of the criteria were rated as unclear

(Table 5). The most common limitations were minimal reporting of appropriate cost measurements (three studies), research questions (two studies), of the chosen time horizons (two studies), and sensitivity analyses of important variables (two studies). In addition, conflicts of interests or ethical issues were not reported in two studies. The ratings of the studies by two assessors (AS, MW) agreed in 97 and 90 per cent of the cases for the CHEC and ECOBIAS tools, respectively.

Discussion

This systematic review provided weak but consistent evidence that adding a weight loss intervention to MSK therapy in comparison to MSK therapy alone is costeffective for individuals with overweight or obesity.

The results in this systematic review are in line with another recent systematic review on combined lifestyle interventions in individuals with overweight or obesity. Hujbers et al. focused only on subacute (more than twelve weeks duration) LBP [47]. Hujbers et al. indeed concluded that these combined lifestyle interventions are likely to be cost-effective [47]. The latter review included three studies, one of which was evaluated in the present systematic review [44]. The two other studies also investigated a combination of different exercise and dietary interventions [47]. Both studies investigated pain as an outcome. However, the conclusion of the Hujbers et al. review was mainly driven by Williams et al., which

Study	CH	EC Li	st—C	Iriteri	а																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19			
Barton et al., 2009 [39]	\checkmark	\checkmark	Ν	\checkmark	\checkmark	\checkmark	\checkmark	Ν	\checkmark													
Harris et al., 2022 [40]	\checkmark	Ν	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	n.a	Ν	\checkmark	\checkmark	Ν	Ν									
Knoop et al., 2023 [41]	\checkmark	Ν	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	n.a	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark									
O'Brien et al., 2018 [42]	\checkmark	\checkmark	\checkmark	\checkmark	Ν	\checkmark	n.a	Ν	\checkmark	\checkmark	\checkmark	\checkmark										
Sevick et al., 2009 [43]	\checkmark	Ν	Ν																			
Williams et al., 2019 [44]	\checkmark	\checkmark	Ν	\checkmark	Ν	\checkmark	n.a	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark										
Study	EC	OBIA	s—c	Criter	ia																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Kopp et al. 2024 [<mark>45</mark>]	\checkmark	\checkmark	Ν	Ν	\checkmark	?	?	?	\checkmark	Ν	Ν	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	?	Ν	\checkmark	Ρ	?
Losina et al., 2019 [46]	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	?	\checkmark	\checkmark	Ν	Ν	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	?	?	Р	\checkmark	Р	?

Table 5 Methodological quality appraisal of included studies: Consensus on Health Economic Criteria (CHEC) and Bias in Economic Evaluation (ECOBIAS) List

N No, n.a. Not applicable, P Partly, ?: Unclear, √: Yes

showed a high probability that the intervention was costeffective [44] (Table 4). In comparison, the present study employed a more extensive search strategy, encompassing all MSK disorders, and standardized all costs to the (Belgium Euros) and price year (2023). This study builds upon the work of Huijbers et al. by analysing a larger population using a more rigorous methodology. However, despite these improvements, the present study found only low-quality evidence for cost-effectiveness across the eight included studies.

Notwithstanding the present systematic review, only one clinical study was identified investigating similar populations and interventions. Kostic et al. used a model-based evaluation to assess the cost-effectiveness of surgical and non-surgical weight loss interventions on individuals with Class III obesity (mean BMI 42.9 to 46.5 kg/m²) who were considering a total knee replacement [38]. The lifestyle intervention included coaching on diet and exercise interventions and the potential use of a weight loss medication (Orlistat). Compared to a Roux-En-Y gastric bypass (RYGB) or a laparoscopic sleeve gastrectomy (LSG), this lifestyle intervention was not cost-effective as it revealed higher ICER values and less QALY gains than those surgeries. No specific values were reported due to the dominance of the other two interventions (ICER for RYGB: \$20'500/QALY (\$US 2020) = €19'225.28 (€2023 Belgium); ICER for LSG: \$10'600/QALY (\$US 2020) =€9'940.87 (€2023 Belgium)) [38].

Different willingness-to-pay thresholds exist depending on the respective country [48]. All available ICUR values from the included studies fall below the reported willingness-to-pay thresholds. This supports our conclusion that the addition of weight loss interventions to usual care is likely to be cost-effective in the studied population. As outlined in the methods section, the net monetary benefit (NMB) was calculated without monetising clinical effects to avoid double counting [23, 32, 33]. Consequently, no willingness-to-pay thresholds were defined in the methods section. The results presented should therefore be interpreted with caution. For instance, in the study by Harris et al. [40], a negative NMB of -79.66 was calculated. However, if a willingness-to-pay threshold were incorporated into this calculation, it would yield a positive NMB.

Limitations and strengths of evidence included in the review

The studies included in this review had some limitations, particularly concerning the long-term effects of the weight loss interventions, since only three studies were conducted over a period greater than one year [39, 43, 46]. Regarding to the cost-related data, the different terminologies used hindered data comparability. Clear definitions for the main cost categories (direct medical, direct non-medical, indirect costs, or total costs) [39, 42– 44] and a reporting of disaggregated values were often absent [39, 46], and CBAs were not found in the systematic, independent literature search of this research area.

On the other hand, strengths of this present systematic review were the relatively recent literature available (published from 2009 to 2024) and the strong methodological quality of the included studies. For example, only two items per study had responses of "no" on the checklists. The only exception was the Harris et al. study, with four items that were answered with "no" [40].

Limitations and strengths of the systematic review process

Limitations exist in the review process used. Firstly, the health systems of the three countries (Australia, the

United States and the United Kingdom) differ [49–51]. In addition, varying MSK diagnoses were investigated, ranging from self-reported knee pain [39] and knee osteoarthritis [40, 42, 43, 46] to LBP [44]. A bias was evident due to the different data collection dates although this was reduced by the conversion used and the relatively short time since the studies were published (2009 to 2024). In addition, differences in the interventions used and their implementation could have contributed to the diversity of the results particularly in terms of the various targets for the dietary interventions, from the specific 600 kilocalories per day of caloric restriction [39] to the more general target of five [40] or ten [41, 42] percent of body weight reduction. Only Harris et al. [40] provided details on dietary interventions, while Barton et al., Sevick et al. and Knoop et al. reported details on exercise interventions [39, 41, 43]. In addition, study protocols and corresponding intervention-oriented publications contained no further information on these matters. Furthermore, study comparison is difficult due to the heterogeneity of control interventions including exercise [39, 43], supplementation with NSAID [46], and waiting for a medical consultation [42, 44]. The use of different quality-of-life questionnaires (EQ-5D [39, 43], Aqol-8D [40], SF-6D [42, 44] or lack of information from data collection [46] sources may also contribute to differences in the results obtained. Secondly, to recalculate the costs included in the studies to 2023 Belgium Euros, the estimated PPP values of the International Monetary Fund for the PPP values were used [52]. No current PPP data were available for 2023 Belgium Euros conversions [52].

Next to these limitations, some strengths are evident. This present systematic review was conducted based on a qualitative reputable literature search that was validated by an experienced external librarian, which, when combined with the independent screening procedure, data extraction and methodological quality assessment conducted by two independent reviewers, reduces the risk of bias. The forward and backward screening did not identify any additional studies, which suggests that all relevant studies were likely identified. Furthermore, comparability was increased due to the conversion of the costs to 2023 Belgium Euros, while the addition of CBA studies reporting disaggregated data improved the data synthesis and reporting. For example, the Harris et al. and Sevick et al. studies appeared to be cost-effective when comparing the diet and exercise intervention to an exercise-based control intervention [40, 43]. The use of the cost-benefit parameters ROI, NMB, and BCR allowed for a more detailed interpretation of the data.

Implications of the results for practice, policy, and future research

This study does not provide sufficient evidence to make generalisable recommendations for clinical practice, largely due to the heterogeneity of the populations, interventions, and controls in the included publications. However, it highlights significant research gaps that warrant further exploration, particularly in costeffectiveness research. Future studies should focus on identifying specific MSK diseases that benefit most from the addition of a weight loss intervention. Additionally, standardisation of both interventions and control treatments is necessary to improve comparability across different MSK diseases and within each disease category, e.g. knee osteoarthritis or chronic low back pain as the most common MSK diagnosis in this population. There should also be a stronger emphasis on study design quality, including the collection of disaggregated cost data, with a focus on indirect costs, which are a major cost driver for individuals with overweight or obesity. These evaluations should consider time horizons of at least one year, or longer if feasible. We therefore recommend conducting multi-year evaluations from a societal perspective that include indirect costs. with detailed documentation and standardisation of interventions, to enhance the relevance and applicability of findings. This approach could also incentivise health insurers to invest in novel and polymodal therapy methods in clinical practice.

Conclusions

The aim of this systematic review was to analyse the costeffectiveness of a weight reduction intervention in addition to MSK treatments compared to MSK treatments alone to alleviate pain and restore function for individuals suffering from overweight or obesity with a musculoskeletal diagnosis. This systematic review included six trial-based and two model-based health economic evaluations with high methodological quality. Based on the number of studies, which show increased, but also reduced costs in some studies alongside additional effects, and supported by ICUR values, the studies indicate a tendency towards cost-effectiveness for the investigated additive weight loss interventions. Difficulties in comparing the studies arose from the large amount of methodological heterogeneity across the included studies regarding the content of the intervention and control groups. The importance of presenting disaggregated costs in health economic evaluations, encompassing both direct and indirect costs, is emphasised. Future studies should examine the long-term cost-effectiveness of nonpharmacological weight loss interventions.

Abbreviations

7.0001011010	
BCR	Benefit-cost-ratio
BMI	Body Mass Index
CBA	Cost-benefit analyses
CEA	Cost-effectiveness analyses
CHEC	Consensus Health economic Criteria
CUA	Cost-utility analyses
ECOBIAS	Bias in economic evaluation
GDP	Gross Domestic Product
ICER	Incremental cost-effectiveness ratios
ICUR	Incremental costs-utility ratios
LBP	Low back pain
LSG	Laparoscopic sleeve gastrectomy
MSK	Musculoskeletal
NMB	Net monetary benefit
PPP	Purchasing power parity values
RYGB	Roux-En-Y gastric bypass
ROI	Return-on-investment
WOMAC	Western Ontario and McMaster Universities osteoarthritis index

Supplementary Information

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Supplementary Material 1.

Authors' contributions

All listed have made the required substantive contributions and therefore meet the criteria for authorship. AS: Project development, conception, design; data collection, screening, data extraction and analyses; manuscript writing, article revision; final approval MW: Data screening, data extraction, article revision; final approval ML: Data screening, data extraction, article revision; final approval RC: Project development; article revision; final approval TD: Project development; article revision; final approval JT: Project development, conception, design; article revision; final approval NL: Project development, conception, design; data analyses; article revision; final approval.

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Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

This is not necessary as it is a systematic review.

Consent for publication

This is not necessary as it is a systematic review.

Competing interests

The authors declare no competing interests.

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