[LITERATURE REVIEW]

EMMA K. ROBSON, BSND[1-4] • REBECCA K. HODDER, PhD[1-4] • STEVEN J. KAMPER, PhD[3,5]
KATE M. O'BRIEN, PhD[1-4] • AMANDA WILLIAMS, PhD[1-3] • HOPIN LEE, PhD[2,3,6] • LUKE WOLFENDEN, PhD[1,2,4]
SERENE YOONG, PhD[1,2,4] • JOHN WIGGERS, PhD[1,2,4] • CHRIS BARNETT, MPhysio[7,8] • CHRISTOPHER M. WILLIAMS, PhD[1-4]

Effectiveness of Weight-Loss Interventions for Reducing Pain and Disability in People With Common Musculoskeletal Disorders: A Systematic Review With Meta-Analysis

Musculoskeletal disorders are a leading cause of disability worldwide.[22] Hip and knee osteoarthritis (OA) and spinal pain (low back and neck pain) together have accounted for 75% of years lived with disability from musculoskeletal disorders in 2016.[22] Spinal pain has accounted for more disability than any other condition globally, totaling 86.5 million years lived with disability.[22] Hip and knee OA have accounted for over 16 million years lived with disability, and have been the 12th leading cause of disability.[22]

• **OBJECTIVE:** To assess the effectiveness of weight-loss interventions on pain and disability in people with knee and hip osteoarthritis (OA) and spinal pain.

• **DESIGN:** Intervention systematic review.

• **LITERATURE SEARCH:** Twelve online databases and clinical trial registries.

• **STUDY SELECTION CRITERIA:** Randomized controlled trials of any weight-loss intervention (eg, diet, physical activity, surgical, pharmaceutical) that reported pain or disability outcomes in people with knee or hip OA or spinal pain.

• **DATA SYNTHESIS:** We calculated mean differences or standardized mean differences (SMDs) and 95% confidence intervals (CIs). We used the Cochrane risk of bias tool to assess risk of bias and the Grading of Recommendations Assessment, Development, and Evaluation tool to judge credibility of evidence.

• **RESULTS:** Twenty-two trials with 3602 participants were included. There was very low– to very low–credibility evidence for a moderate effect of weight-loss interventions on pain intensity (10 trials, n = 1806; SMD, –0.54; 95% CI: –0.86, –0.22; I^2 = 87%, $P<.001$) and a small effect on disability (11 trials, n = 1821; SMD, –0.32; 95% CI: –0.49, –0.14; I^2 = 58%, $P<.001$) compared to minimal care for people with OA. For knee OA, there was low- to moderate-credibility evidence that weight-loss interventions were not more effective than exercise only for pain intensity and disability, respectively (4 trials, n = 673; SMD, –0.13; 95% CI: –0.40, 0.14; I^2 = 55%; 5 trials, n = 737; SMD, –0.20; 95% CI: –0.41, 0.00; I^2 = 32%).

• **CONCLUSION:** Weight-loss interventions may provide small to moderate improvements in pain and disability for OA compared to minimal care. There was limited and inconclusive evidence for weight-loss interventions targeting spinal pain. *J Orthop Sports Phys Ther 2020;50(6):319-333. Epub 9 Apr 2020. doi:10.2519/jospt.2020.9041*

• **KEY WORDS:** *management, musculoskeletal, obesity*

Up to 45% of the burden from OA and spinal pain has been attributed to overweight or obesity.[8] People with OA who are overweight or obese have 3 times increased odds of worsening knee OA.[44] People who are overweight or obese and have spinal pain have up to 1.4 times increased odds of persistent back pain[52] compared to those of normal weight. There is low-quality evidence that reducing body weight by 5% is associated with meaningful improvements in pain and disability in people who are overweight and have OA.[13] Weight loss is widely recommended as a treatment approach to improve pain and disability in people with OA and spinal pain who are overweight or obese.[29,40,47]

There are many weight-loss approaches for people who are overweight (including behavioral interventions targeting diet and/or physical activity and surgical and pharmaceutical interventions).

[1]Hunter New England Population Health, Hunter New England Local Health District, Wallsend, Australia. [2]School of Medicine and Public Health, University of Newcastle, Callaghan, Australia. [3]Centre for Pain, Health and Lifestyle, Australia. [4]Hunter Medical Research Institute, New Lambton Heights, New South Whales, Australia. [5]School of Public Health, University of Sydney, Camperdown, Australia. [6]Centre for Statistics in Medicine and Centre for Rehabilitation Research in Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom. [7]John Hunter Hospital, Hunter New England Local Health District, New Lambton Heights, Australia. [8]School of Physiotherapy, University of Newcastle, Callaghan, Australia. This study was prospectively registered with PROSPERO (registration number CRD42016043134). This work was not supported by any external grants or funding. The authors certify that they have no affiliations with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the article. Address correspondence to Emma K. Robson, Hunter New England Population Health, Locked Bag 10, Wallsend, NSW 2287 Australia. E-mail: emma.robson@health.nsw.gov.au

However, systematic reviews of weight-loss interventions for people with musculoskeletal conditions have only included behavioral (diet and physical activity) interventions.[4,13,17] People with musculoskeletal conditions may face specific barriers to engaging in behavioral weight-loss interventions, including those targeting physical activity, due to obesity or pain that impacts everyday activity.[17,21] Comprehensive synthesis of all weight-loss interventions for people with musculoskeletal conditions is needed to help clinicians and patients make decisions about weight-loss treatment options.

The aim of this study was to assess the effectiveness of weight-loss interventions (including behavioral, pharmaceutical, surgical, and cognitive/psychological strategies) for reducing pain and disability in people with hip or knee OA or spinal pain.

METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[51] and was prospectively registered with PROSPERO (registration number CRD42016043134).

Data Sources and Searches

We searched MEDLINE, MEDLINE In-Process, AMED, CINAHL, the Cochrane NHS Economic Evaluation Database, the Cochrane Central Register of Controlled Trials, Embase, PsycINFO, and SPORTDiscus on February 5, 2019. The search strategy (**APPENDIX A**, available at www.jospt.org) was drafted in consultation with an information specialist and adapted for each database. We searched clinical trial registries in February 2019 (www.ClinicalTrials.gov, the Australian New Zealand Clinical Trials Registry, and the World Health Organization International Clinical Trials Registry Platform) to identify ongoing trials. We hand searched reference lists and contacted the authors of included studies to identify additional trials.

Trial Selection

We included randomized controlled trials (RCTs) and cluster randomized controlled trials (C-RCTs) with parallel groups. There was no restriction on language or publication date.

Participants

We included trials that recruited participants with a primary complaint of hip or knee OA or spinal pain (low back or neck pain). Diagnosis of hip or knee OA could be radiographic or clinical.[5,6,62] We excluded trials that recruited participants with hip or knee pain but no stated diagnosis of OA. We defined low back pain as pain located in the back between the 12th rib and buttock crease, with or without leg pain.[31] We defined neck pain as pain located in the cervical region of the spine.[16,27] We excluded trials with participants who had pain as a result of serious underlying conditions such as fracture, infectious disease, cancer, or systemic inflammatory conditions (eg, rheumatoid arthritis). We only included trials of mixed conditions when data were reported separately for OA and spinal pain. We placed no restriction on participant age.

Intervention

We included trials that assessed the effect of any intervention with a stated intention of reducing weight, regardless of the content, delivery methods, providers, intensity, or duration. This could include pharmacological, surgical, behavioral (diet and/or physical activity), or cognitive and psychological strategies. We excluded trials in which only a proportion of participants in an intervention arm were offered a weight-loss intervention. Trials that measured or reported on "weight" or "weight loss" but did not report weight loss as an intended treatment target were excluded, for example, therapeutic exercise interventions aiming to increase fitness or strength that did not explicitly aim to reduce weight.

Comparator

A comparison group could be any inactive or active control, including no care, wait list, minimal intervention, usual care, placebo or sham intervention, or an alternative intervention (eg, therapeutic exercise intervention).

Outcomes

We included a trial of OA (knee or hip) or spinal pain if it reported the effects of the intervention on pain intensity and disability outcomes, our primary outcomes of interest. When trials reported more than 1 pain or disability measure, we used the highest listed measure from a published hierarchy of patient-reported outcomes for meta-analyses, detailed for OA.[30] For spinal pain, we used the most valid and frequently used measure agreed on by consensus of the review authors.

Secondary outcomes captured for the review were weight, body mass index, physical performance measures, physical activity, dietary outcomes, mental health, and quality of life. We included physical performance outcomes measured by the 6-minute walk test or timed up-and-go test,[1] in line with the Osteoarthritis Research Society International recommendations[18] for assessing OA outcomes. We extracted both observer-rated and self-reported measures, prioritizing the former for extraction and inclusion in meta-analyses.

Data Extraction

Pairs of reviewers independently screened titles and abstracts, and then full texts, of potentially eligible papers. Reviewers resolved disagreements by consensus or a third reviewer when a consensus could not be reached. We contacted authors for translations of potentially eligible non-English trial reports and, when they did not reply, used Google Translate to screen the article against the eligibility criteria.

Two reviewers independently extracted data on trial design, participant characteristics, intervention description, outcome measures, and outcome data using a standardized data-extraction form. Discrepancies were resolved by consensus or, where necessary, by a third reviewer. We contacted trial authors where

important data were missing or information was required to determine eligibility.

Risk of Bias Across Trials

We used the Cochrane Collaboration risk of bias tool (Version 1) to assess random sequence generation, allocation concealment, blinding, incomplete data, selective reporting, and any other sources of bias such as contamination.[25] We additionally assessed C-RCTs for recruitment bias, baseline imbalance, loss of clusters, and incorrect analysis.[25] Two reviewers independently assessed each trial, with input from a third reviewer for unresolved differences. Trials were categorized as high risk of bias if they had high risk of bias in 3 or more of the 6 domains.

Data Synthesis and Analysis

We conducted meta-analysis based on condition (OA, including hip and knee, or spinal pain) when there were 2 or more trials for a condition, regardless of statistical heterogeneity. We performed separate meta-analyses for different comparators. We grouped trials with no- or low-intensity comparators as "minimal care." Minimal care could be usual care, attention or wait-list controls, placebo, a minimal intervention such as brief education or advice about self-management, or generic healthy lifestyle advice.

We grouped similar active comparators, irrespective of the dose or delivery (eg, exercise). When trials had more than 2 comparison arms, per Cochrane recommendations we combined similar intervention arms (active interventions) to form one comparison for the primary meta-analyses (eg, different types of exercise such as land-based and aquatic exercise weight-loss interventions). Where intervention arms were dissimilar (eg, dietary weight loss plus exercise versus dietary weight loss only), the number of participants in the control group was divided by the number of intervention arms to enable separate comparisons.[25] We used the first postintervention completion data point for synthesis in meta-analyses.

We calculated the mean difference and 95% confidence interval (CI) where trials reported the same outcome measure, and the standardized mean difference (SMD) where different outcome measures were reported. We used random-effects models, as we expected heterogeneity, and generic inverse variance methods to accommodate the inclusion of both RCTs and C-RCTs.[25] We assessed C-RCTs for unit-of-analysis errors. If clustering was not appropriately handled or intraclass correlation coefficients were not reported or supplied by the authors, then we adjusted for clustering.[25] We conducted meta-analyses using Review Manager Version 5.3.5 (The Nordic Cochrane Center, Copenhagen, Denmark).

We interpreted the effect size for the SMD according to Cohen's d (0.2, small effect; 0.5, moderate effect; greater than 0.8, large effect).[15] To facilitate interpretation, we transformed the SMD to provide an estimate of the mean difference for the primary outcomes (pain and disability) and weight outcomes. To do so, we used the most valid, widely used measurement tool of the included trials[25] and multiplied the SMD by the standard deviation of the combined groups at baseline of the trial that had the lowest risk of bias and used the tool. Data from trials not included in meta-analyses were presented separately.

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria to assess the credibility of evidence for each meta-analysis.[24] The credibility of evidence (categorized as "high," "moderate," "low," or "very low") was downgraded from high, based on limitations of the trial design, inconsistency of the results, imprecision, indirectness, or publication bias. Publication bias was assessed via visual inspection of funnel plots.

Subgroup and Sensitivity Analysis

We conducted subgroup analyses by intervention type and duration, where possible, for pain, disability, and weight outcomes. Intervention types were defined as multifocused interventions with weight loss, where weight loss was a component of a broader, pain-focused intervention (eg, with advice/education or cognitive or psychological pain management strategies), or weight loss–only interventions, where the entire intervention was focused on weight loss (eg, appetite suppressants, meal replacements, reduced-calorie diets with or without exercise) without any additional components. There were insufficient trials with similar comparison groups to conduct subgroup analyses by specific intervention type, such as pharmaceuticals, meal replacements, etc. Trials were defined as having a duration of less than 12 months or 12 months or greater.

We performed sensitivity analysis to explore the influence of bias by removing trials with an overall high risk of bias. We assessed statistical heterogeneity using the I^2 statistic, where a score greater than 75% was considered high.[26] We attempted to investigate the sources of high heterogeneity (greater than 75%) for primary outcomes by examining I^2 values in subgroup analyses by intervention type. Evidence credibility was downgraded for unexplained heterogeneity.

Protocol Deviations

We included only RCTs to ensure the highest-quality evidence. We added physical performance measures as an outcome. We presented a summary table of trials not included in the meta-analysis, instead of qualitative synthesis, due to the large number of outcomes.

RESULTS

We identified 8889 unique records, of which 268 full texts were reviewed and 22 trials (18 RCTs[10-12,14,23,28,33-39,41,45,46,53,54,56,59-61] and 4 C-RCTs[2,3,7,43,50] in 44 records) were included (**FIGURE 1**, **TABLE 1**; full details of interventions are presented in **APPENDIX B**, available at www.jospt.org). **TABLE 2** shows the results of the 16 trials included in meta-analyses, and the 6 trials that were not, and addi-

tional outcomes not included in the meta-analysis are provided in **APPENDIX B**.

Trial Characteristics

There were 19 trials that included 3310 participants with either knee OA (n = 17)[10-12,14,23,33-38,41,43,45,46,50,53,54,56,60,61] or knee and hip OA (n = 2),[2,3] and 3 trials that included 292 participants with chronic low back pain.[28,39,59] Intervention durations ranged from 6 weeks to 3 years. All but 1 trial reported follow-up immediately post intervention.[53] Only 2 trials collected long-term follow-up data (up to 11 months post intervention).[7,43,50] Seventeen trials (OA, n = 15; spinal pain, n = 2) examined weight loss–only interventions including diet-only interventions (reduced-calorie diets with or without meal replacements),[10,11,23,34,36,46,54,60] exercise interventions,[33,61] combined diet and exercise interventions,[23,28,34-36,38,41,53,60] and pharmaceutical interventions.[39,54,56] Six trials (OA, n = 5; spinal pain, n = 1) examined multifocused interventions with weight loss, including telephone coaching for weight loss combined with cognitive behavioral therapy, specialist referral,[2,3] or spinal pain education[59]; and diet and exercise interventions combined with OA education[43,50] or psychological pain-coping interventions.[53] Trial comparator groups included attention control, placebo, usual care, exercise only, diet only, therapeutic exercise, or brief lifestyle education.

Adherence to interventions (based on session attendance, calls completed, meal replacements consumed) ranged from 34% to 100% for weight loss–only interventions and from 45% to 95% for multifocused interventions. Interventions delivered via telephone had the lowest average adherence (34% to 46% of completed sessions). Interventions using diet and exercise approaches, either combined or independently, had average adherence rates between 70% and 73% of sessions completed. Only 1 of 3 pharmaceutical trials reported adherence, which was 100% of the prescribed medication.[54]

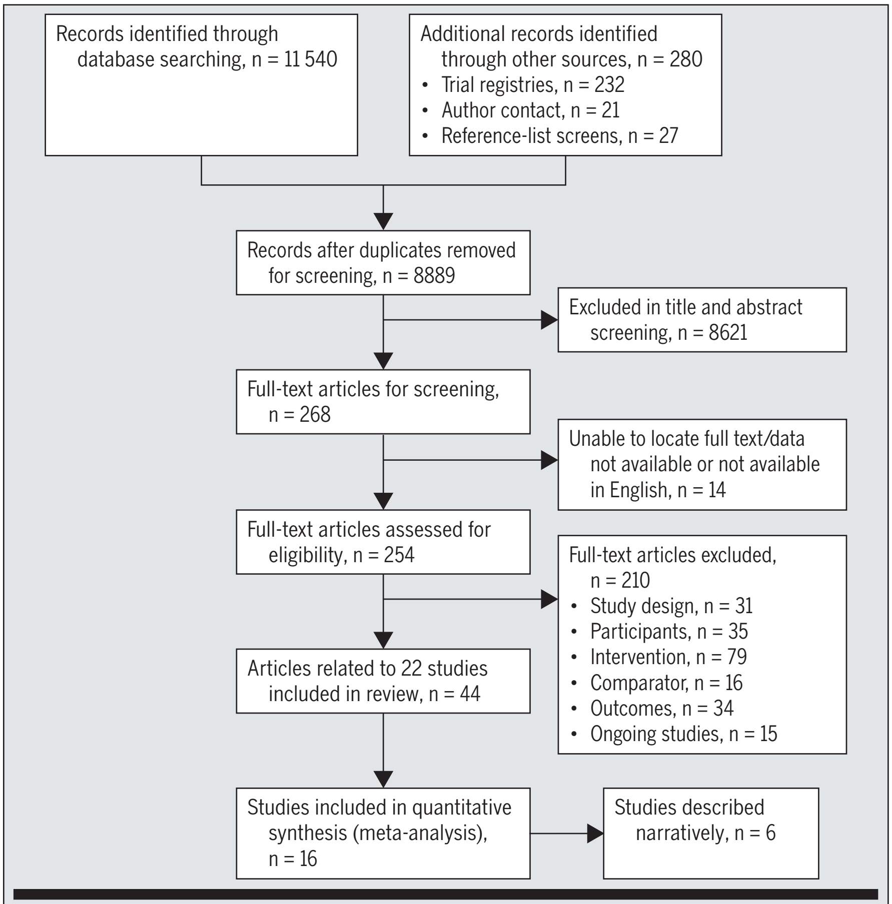


FIGURE 1. PRISMA flow diagram for the process of trial selection.

Risk of Bias Across Trials

We judged 7 trials as having a high overall risk of bias (**FIGURE 2**). Due to the nature of interventions and outcomes (self-report), almost all trials were at high risk of bias for blinding. Two trials had a high risk of bias for not randomizing group selection or selection bias, 2 for allocation concealment, and 7 for incomplete outcome data (attrition bias). Two trials were at high risk of recruitment bias or bias due to having no adjustment for clustering.

Results of Meta-Analyses

All meta-analyses, including primary and secondary outcomes, are reported in **TABLE 2** and **APPENDICES C**, **D**, and **E**.

Weight-Loss Interventions Versus Minimal Care (Hip and Knee OA) There was very low–credibility evidence from 10 trials[2,3,23,33,34,38,41,43,50,53] (n = 1806) for a moderate effect of weight-loss interventions (including diet and exercise, diet only, exercise only, and multifocused interventions) on pain intensity compared to minimal care (SMD, –0.54; 95% CI: –0.86, –0.22; I^2 = 87%) (**FIGURE 3**, **TABLE 2**). This equated to an estimated mean difference of –1.77 points on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale or of –1 points on a 0-to-10 numeric pain-rating scale. There was no effect on pain intensity when trials at high risk of bias were removed from the meta-analyses (SMD, –0.32; 95% CI: –0.68, 0.04) (**APPENDIX C**, available at www.jospt.org; **TABLE 2**).

Subgroup analysis showed a large effect of multifocused interventions (SMD, –0.81; 95% CI: –1.41, –0.21; I^2 = 94%) and a small effect of weight loss–only interventions (SMD, –0.36; 95% CI: –0.71, –0.01; I^2 = 72%) on pain (**FIGURE 3**, **TABLE 2**) compared to minimal care. The

interaction term for the subgroup analysis was not significant. Subgroup analysis showed a small effect of weight-loss interventions of less than 12 months' duration (SMD, –0.85; 95% CI: –1.39, –0.30; I^2 = 91%), and no effect of interventions lasting 12 months or longer (SMD, –0.13; 95% CI: –0.28, 0.02; I^2 = 0%) (**TABLE 2**). The interaction term for the subgroup analysis was significant.

There was low-credibility evidence from 11 trials[2,3,23,33,34,38,41,43,53,56,60] (n = 1821) for a small effect of weight-loss interventions (including diet and exercise, diet only, exercise only, multifocused, and pharmaceutical interventions) on disability compared to minimal care (SMD, –0.32; 95% CI: –0.49, –0.14; I^2 = 58%) (**FIGURE 3**, **TABLE 2**). This equated to an estimated mean difference of –3.7 points on the WOMAC function subscale. Effects were similar when trials at high risk of bias were removed from the analysis (**APPENDIX C**, **TABLE 2**).

Subgroup analysis showed small effects of weight loss–only interventions (SMD, –0.40; 95% CI: –0.69, –0.12; I^2

TABLE 1 Characteristics of Included Trials

Study/Type/Country/Trial	Condition/BMI/Arms	Length of Follow-up/Lost to Follow-up/Intervention Adherence	Primary/Secondary Outcomes
Allen et al[3] C-RCT United States	Knee/hip OA (n = 300) >25 kg/m² 2 arms	12 mo 9% NR	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) BMI, mental health (PHQ), physical activity (CHAMPS)
Allen et al[2] C-RCT United States	Knee and/or hip OA (n = 537) >25 kg/m² 4 arms	12 mo 19.1% Patients, 43%; providers, 47% of calls completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) BMI, mental health (PHQ), physical activity (CHAMPS)
Bliddal et al,[10] Christensen et al[12] RCT Denmark	Knee OA (n = 96) >28 kg/m² 2 arms	12 mo 41.7% 58% completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms)
Christensen et al[11] RCT Denmark LIGHT	Knee OA (n = 153) >30 kg/m² 2 arms	3 y 29.5% 70% of sessions completed	Pain (KOOS pain subscale) and disability (KOOS function in sport and recreation subscale) Weight (kilograms), KOOS knee-related QoL subscale
Ghroubi et al[23] RCT France	Knee OA (n = 56) >30 kg/m² 4 arms	8 wk 19.7% NR	Pain (VAS) and disability (WOMAC) Weight (kilograms), physical performance (6MW)
Irandoust et al[28] RCT Iran	LBP (n = 36) NR 2 arms	4 mo NR NR	Pain (VAS) Weight (kilograms)
Lim et al[33] RCT the Netherlands	Knee OA (n = 75) >25 kg/m² 3 arms	8 wk 12% Aquatic, 92%; land, 88% of sessions completed	Pain (BPI, 0-11) and disability (WOMAC) Weight (kilograms), mental health (SF-36 MCS)
Messier et al[35] RCT United States	Knee OA (n = 24) >28 kg/m² 2 arms	6 mo 12.5% Diet plus exercise, 95% of sessions completed	Pain (knee pain scale, ambulation intensity of 0-6) and disability (FAST Functional Performance Inventory) Weight (kilograms), physical performance (6MW)
Messier et al,[34] Rejeski et al[45] RCT United States ADAPT	Knee OA (n = 316) >28 kg/m² 4 arms	18 mo 20.3% Diet, 72%; exercise, 60%; diet plus exercise, 64% of sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW), mental health (SF-36 MCS)
Messier et al[36] RCT United States IDEA	Knee OA (n = 454) >27-41 kg/m² 3 arms	18 mo 12.2% Diet, 61%; diet plus exercise, 63% of sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW), mental health (SF-36 MCS)
Miller et al[37,38] RCT United States	Knee OA (n = 87) >30 kg/m² 2 arms	6 mo 9.2% Intervention group, 77% of exercise and 75% of nutrition sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW)
Muehlbacher et al[39] RCT Germany	CLBP (n = 96) NR 2 arms	10 wk 8.4% NR	Pain (PRI of the MPQ, 0-40) and disability (ODQ) Weight (kilograms), mental health (SF-36 MCS)

Table continues on page 324.

TABLE 1 CHARACTERISTICS OF INCLUDED TRIALS (CONTINUED)

Study/Type/Country/Trial	Condition/BMI/Arms	Length of Follow-up/Lost to Follow-up/ Intervention Adherence	Primary/Secondary Outcomes
O'Brien et al[41]	Knee OA (n = 120)	6 mo	Pain (NRS, 0-10) and disability (WOMAC function subscale)
RCT	27-40 kg/m^2	12%	Weight (kilograms), mental health (SF-12 Version 2 MCS), physical activity (MVPA), dietary intake (FFQ)
Australia	2 arms	34% completed ≥6 calls	
Ravaud et al[43]	Knee OA (n = 336)	4 mo	Pain (NRS, 0-10) and disability (WOMAC function subscale)
C-RCT	25-35 kg/m^2	12.3%	Weight (kilograms), mental health (SF-12 MCS)
France	2 arms	95% attended 3 consultations	
ARTIST			
Riecke et al[46]	Phases 1 and 2: knee OA (n = 192)	68 wk	Pain (OMERACT-OARSI VAS, 0-100) and disability (OMERACT-OARSI VAS, 0-100)
RCT (phase 1 of 2)		12.7%	
Christensen et al[14]	NR	90% of sessions completed	Weight (kilograms), mental health (SF-36 MCS), KOOS knee-related QoL subscale
RCT (phase 2 of 2)	Phase 1, 2 arms; phase 2, 3 arms		
Denmark			
Aree-Ue et al,[7] Saraboon et al[50]	Knee OA (n = 80)	8 wk	Pain (NRS, 0-10)
C-RCT	23-29 kg/m^2	NR	Weight (kilograms), physical performance (TUG)
Thailand	2 arms	NR	
Somers et al[53]	Knee OA (n = 232)	PTA, 24 wk plus 6 mo plus 12 mo	Pain (WOMAC pain subscale) and disability (WOMAC function subscale)
RCT	25-42 kg/m^2	29.75%	Weight (pounds), mental health (AIMS psychological scale)
United States	4 arms	BWM, 65%; PCST plus BWM, 73% of sessions completed	
Strebkova and Alekseeva[54]	Knee OA (n = 50)	6 mo	Pain (WOMAC pain VAS, 0-100) and disability (WOMAC function VAS, 0-100)
RCT	>30 kg/m^2	0%	Weight (kilograms)
Russia	2 arms	100% drug compliance	
Toda et al[56]	Knee OA (n = 40)	6 wk	Disability (Lequesne index of severity)
RCT	>26.4 kg/m^2	7.5%	Weight (kilograms), physical activity (steps per day)
Japan	2 arms	NR	
Williams et al[59]	CLBP (n = 160)	26 wk	Pain (NRS, 0-10) and disability (RMDQ)
RCT	27-40 kg/m^2	21.8%	Weight (kilograms), mental health (SF-12 Version 2 MCS), physical activity (MVPA), dietary intake (FFQ)
Australia	2 arms	41% completed ≥6 calls	
Wolf et al[60]	Knee OA (n = 110)	24 wk	Disability (WOMAC function subscale)
RCT	NR	22%	Weight (pounds), physical performance (6MW), mental health (SF-36 MCS)
United States	4 arms	NR	
Yázigi[61]	Knee OA (n = 52)	12 wk	Pain (BPI) and disability (KOOS)
RCT	NR	7.7%	Weight (kilograms), KOOS knee-related QoL subscale
Portugal	2 arms	NR	

Abbreviations: 6MW, 6-minute walk; ADAPT, Arthritis, Diet, and Activity Promotion Trial; AIMS, Arthritis Impact Measurement Scales; ARTIST, osteoarthritis intervention standardized; BMI, body mass index; BPI, Brief Pain Inventory; BWM, behavioral weight management; CHAMPS, Community Healthy Activities Model Program for Seniors; CLBP, chronic low back pain; C-RCT, cluster randomized controlled trial; FAST, Fitness Arthritis and Seniors Trial; FFQ, Food Frequency Questionnaire; IDEA, Intensive Diet and Exercise for Arthritis; KOOS, Knee injury and Osteoarthritis Outcome Score; LBP, low back pain; LIGHT, Long-term Intervention With Weight Loss in Patients With Concomitant Obesity and Knee Osteoarthritis; MCS, mental component summary; MPQ, McGill Pain Questionnaire; MVPA, moderate to vigorous physical activity; NR, not reported; NRS, numeric rating scale; OA, osteoarthritis; OARSI, Osteoarthritis Research Society International; ODQ, Oswestry Low Back Pain Disability Questionnaire; OMERACT, Outcome Measures in Rheumatology; PCST, pain coping skills training; PHQ, Patient Health Questionnaire; PRI, Pain Rating Index; PTA, posttreatment average; QoL, quality of life; RCT, randomized controlled trial; RMDQ, Roland-Morris Disability Questionnaire; SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; TUG, timed up and go; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

= 64%) and multifocused interventions (SMD, –0.24; 95% CI: –0.42, –0.05; I^2 = 43%) on disability compared to minimal care (**FIGURE 3**, **TABLE 2**). The interaction term for the subgroup analysis was not significant. Subgroup analysis showed a small effect of weight-loss interventions of less than 12 months' duration (SMD, –0.46; 95% CI: –0.74, –0.18; I^2 = 91%) and no effect of interventions lasting 12 months or longer (SMD, –0.18; 95% CI: –0.33, –0.03; I^2 = 0%) (**TABLE 2**). The interaction term for the subgroup analysis was significant.

There was very low–credibility evidence from 12 trials[2,3,23,33,34,38,41,43,50,53,56,60] (n = 1903) for a small effect of weight-loss interventions (including diet and

exercise, diet only, exercise only, multifocused, and pharmaceutical interventions) on weight compared to minimal care (SMD, −0.42; 95% CI: −0.64, −0.19; I^2 = 77%) (**FIGURE 3**, **TABLE 2**). This equated to a mean difference of −5.6 kg.

Subgroup analysis found a moderate effect of weight loss–only interventions on weight (SMD, −0.56; 95% CI: −0.97, −0.15; I^2 = 83%) and a small effect of multifocused interventions (SMD, −0.21; 95% CI: −0.34, −0.08; I^2 = 1%) compared to minimal care (**FIGURE 3**, **TABLE 2**). The interaction term for the subgroup analysis was not significant.

Weight Loss–Focused Interventions Versus Exercise Only (Knee OA) There was low-credibility evidence from 4 trials[23,34-36] (n = 673) that weight-loss interventions had no effect on pain intensity compared to exercise-only interventions (SMD, −0.13; 95% CI: −0.40, 0.14; I^2 = 55%) (**APPENDIX D**, **TABLE 2**). There were no effects on pain intensity when trials at high risk of bias were removed from the analysis (**APPENDIX C**, **TABLE 2**).

There was moderate-credibility evidence from 5 trials[23,34-36,60] (n = 737) that weight-loss interventions had no effect on disability compared to exercise-only interventions (SMD, −0.20; 95% CI: −0.41, 0.00; I^2 = 32%) (**APPENDIX D**, **TABLE 2**). There were no effects on disability when trials at high risk of bias were removed from the analysis (**APPENDIX C**, **TABLE 2**).

There was low-credibility evidence from 5 trials[23,34-36,60] (n = 714) of a small effect of weight-loss interventions on weight compared to exercise only (SMD, −0.23; 95% CI: −0.39, −0.08; I^2 = 0%) (**APPENDIX D**, **TABLE 2**). This equated to an estimated mean difference of −3.5 kg.

Diet Plus Exercise Versus Diet Only (Knee OA) There was moderate-credibility evidence from 3 trials[23,34,36] (n = 435) of a small effect of combined diet (meal replacements and/or reduced-calorie diets) and exercise interventions on pain intensity compared to diet-only interventions (SMD, −0.48; 95% CI: −0.94, −0.03; I^2 = 75%) (**APPENDIX D**, **TABLE 2**). This equated to an estimated mean difference of −1.5 points on the WOMAC pain subscale.

There was moderate-credibility evidence from 4 trials[23,34,36,60] (n = 476) of a small effect of combined diet and exercise weight-loss interventions on disability compared to diet-only interventions (SMD, −0.38; 95% CI: −0.76, 0.00; I^2 = 67%) (**APPENDIX D**, **TABLE 2**). This equated to an estimated mean difference of −4.1 points on the WOMAC function subscale.

	1	2	3	4	5	6	7
Allen et al[3]	+	?	−	−	+	+	+
Allen et al[2]	+	?	−	−	+	+	+
Christensen et al[12]	?	+	−	−	−	?	+
Christensen et al[11]	+	+	−	−	−	+	?
Ghroubi et al[23]	?	?	?	?	−	+	+
Irandoust et al[28]	?	?	?	−	?	−	?
Lim et al[33]	?	−	−	−	+	?	+
Messier et al[35]	?	?	−	−	+	?	+
Messier et al[34]	+	?	−	−	−	+	+
Messier et al[36]	?	?	−	−	+	+	+
Miller et al[38]	?	?	−	−	+	?	+
Muehlbacher et al[39]	+	?	+	−	+	?	+
O'Brien et al[41]	+	+	+	−	+	+	?
Ravaud et al[43]	−	−	−	−	−	+	−
Riecke et al[46]	+	+	+	−	+	+	+
Saraboon et al[50]	?	+	−	−	+	?	−
Somers et al[53]	+	+	−	−	−	+	+
Strebkova and Alekseeva[54]	?	?	−	−	?	+	+
Toda et al[56]	−	?	−	?	+	?	+
Williams et al[59]	+	+	?	−	+	+	+
Wolf et al[60]	?	?	?	?	−	+	+
Yázigi[61]	?	?	−	−	+	+	+

+ Yes ? Unclear − No

FIGURE 2. Summary of risk-of-bias assessment for included trials. 1, Random sequence generation (selection bias); 2, Allocation concealment (selection bias); 3, Blinding of participants and personnel (performance bias); 4, Blinding of outcome assessment (detection bias); 5, Incomplete outcome data (attrition bias); 6, Selective reporting (reporting bias); 7, Other bias.

TABLE 2 SUMMARY OF META-ANALYSIS RESULTS FOR PRIMARY AND SECONDARY OUTCOMES AND OF SUBGROUP AND SENSITIVITY ANALYSES

Analysis	Patients (Trials), n	SMD[a]	Re-expression of SMD for Overall Result	GRADE
All Weight-Loss Interventions Versus Minimal Care for OA				
Pain	1806 (10)	−0.54 (−0.86, −0.22)	WOMAC pain subscale, −1.77 points; NRS (0-10), −1 points	Very low[b-d]
Weight loss only	614 (6)	−0.36 (−0.71, −0.01)		
Multifocused	1192 (5)	−0.81 (−1.41, −0.21)		
Excluding high ROB	925 (5)	−0.32 (−0.68, 0.04)		
<12 mo in duration	873 (7)	−0.85 (−1.39, −0.30)		
≥12 mo in duration	761 (3)	−0.13 (−0.28, 0.02)		
Disability	1821 (11)	−0.32 (−0.49, −0.14)	WOMAC function subscale, −3.7 points	Low[b,d]
Weight loss only	709 (8)	−0.40 (−0.69, −0.12)		
Multifocused	1112 (4)	−0.24 (−0.42, −0.05)		
Excluding high ROB	1020 (7)	−0.43 (−0.73 −0.13)		
<12 mo in duration	888 (8)	−0.46 (−0.74, −0.18)		
≥12 mo in duration	761 (3)	−0.18 (−0.33, −0.03)		
Weight	1903 (12)	−0.42 (−0.64, −0.19)	−5.6 kg	Very low[b-d]
Weight loss only	711 (8)	−0.56 (−0.97, −0.15)		
Multifocused	1192 (5)	−0.21 (−0.34, −0.08)		
<12 mo in duration	970 (9)	−0.57 (−0.91, −0.23)		
≥12 mo in duration	761 (3)	−0.13 (−0.27, 0.02)		
Physical performance	478 (5)	1.0 (0.44, 1.56)	...	Very low[b,c,e]
Mental health	1780 (8)	0.01 (−0.16, 0.18)	...	Moderate[b,e]
Physical activity	1221 (5)	1.11 (0.34, 1.88)	...	Very low[b-e]
Weight Loss–Focused Interventions Versus Exercise for Knee OA				
Pain	673 (4)	−0.13 (−0.40, 0.14)	No effect	Low[b,e]
Excluding high ROB	435 (3)	−0.04 (−0.48, 0.40)		
Disability	737 (5)	−0.20 (−0.41, 0.00)	No effect	Moderate[b]
Excluding high ROB	499 (4)	−0.18 (−0.49, 0.14)		
Weight	714 (5)	−0.23 (−0.39, −0.08)	−3.5 kg	Low[b,e]
Physical performance, m[f]	729 (5)	−10.47 (−32.2, 11.3)	...	Low[b,e]
Mental health[f]	673 (3)	0.20 (−0.84, 1.25)	...	Low[b,e]

Table continues on page 327.

There was low-credibility evidence from 4 trials[23,34,36,60] (n = 467) of no effect of combined diet and exercise interventions on reducing weight (mean difference, 0.46 kg; 95% CI: −2.55, 3.48; I^2 = 38%) (**APPENDIX D**, **TABLE 2**) compared to diet-only interventions.

Diet Plus Exercise Versus Exercise Only (Knee OA) There was moderate-credibility evidence from 4 trials[23,34-36] (n = 455) of a small effect of combined diet (meal replacements and/or reduced-calorie diets) and exercise interventions on pain intensity compared to exercise-only interventions (SMD, −0.29; 95% CI: −0.55, −0.03; I^2 = 30%) (**APPENDIX D**, **TABLE 2**). This equated to an estimated mean difference of −0.9 points on the WOMAC pain subscale.

There was moderate-credibility evidence from 5 trials[23,34-36,60] (n = 498) of a small effect of combined diet and exercise weight-loss interventions on disability compared to exercise-only interventions (SMD, −0.38; 95% CI: −0.55, −0.20; I^2 = 0%) (**APPENDIX D**, **TABLE 2**). This equated to an estimated mean difference of −4.1 points on the WOMAC function subscale.

There was moderate-credibility evidence from 5 trials[23,34-36,60] (n = 476) of no effect of combined diet and exercise interventions on reducing weight (SMD, −0.21 kg; 95% CI: −0.45, 0.02; I^2 = 25%) (**APPENDIX D**, **TABLE 2**) compared to exercise-only interventions.

Weight-Loss Interventions Versus Minimal Care (Chronic Low Back Pain) Meta-analyses of 2 trials[39,59] for chronic low back pain found no effects for pain intensity (low credibility of evidence), disability (low credibility of evidence), or weight (moderate credibility of evidence) compared to minimal care (**APPENDIX D**, **TABLE 2**). Based on the unusually large effect size for pain in the pharmaceutical trial[39] and the scale used for pain, we suspect that the reported standard deviation may be incorrect, but we were unable to confirm this with the study authors.

TABLE 2 Summary of Meta-Analysis Results for Primary and Secondary Outcomes and of Subgroup and Sensitivity Analyses (continued)

Analysis	Patients (Trials), n	SMD[a]	Re-expression of SMD for Overall Result	GRADE
Dietary Weight Loss and Exercise Versus Dietary Weight Loss Only for Knee OA				
Pain	435 (3)	−0.48 (−0.94, −0.03)	WOMAC pain subscale, −1.5 points	Moderate[b]
Disability	476 (4)	−0.38 (−0.76, 0.00)	WOMAC function subscale, −4.1 points	Moderate[b]
Weight, kg[f]	467 (4)	0.46 (−2.55, 3.48)	No effect	Low[b,e]
Physical performance, m[f]	448 (4)	51.83 (43.7, 59.95)	...	Low[b,e]
Mental health[f]	448 (3)	−0.02 (−1.36, 1.32)	...	Low[b,e]
Dietary Weight Loss and Exercise Versus Exercise Only for Knee OA				
Pain	455 (4)	−0.29 (−0.55, −0.03)	WOMAC pain subscale, −0.9 points	Moderate[b]
Disability	498 (5)	−0.38 (−0.55, −0.20)	WOMAC function subscale, −4.1 points	Moderate[b]
Weight	476 (5)	−0.21 (−0.45, 0.02)	No effect	Moderate[b]
Physical performance, m[f]	466 (5)	14.68 (6.70, 22.66)	...	Low[b,e]
Mental health[f]	446 (3)	0.04 (−0.14, 0.23)	No effect	Low[b,e]
Weight-Loss Interventions Versus Usual Care for Chronic Low Back Pain				
Pain	255 (2)	−3.05 (−8.68, 2.58)	No effect	Low[c,e]
Disability	189 (2)	−0.51 (−1.29, 0.27)	No effect	Low[c,e]
Weight[f]	213 (2)	−2.65 (−7.50, 2.20)	No effect	Moderate[e]
Mental health	200 (2)	−0.38 (−1.47, 0.70)	Not applicable	Low[c,e]

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; NRS, numeric rating scale; OA, osteoarthritis; ROB, risk of bias; SMD, standardized mean difference; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[a]*Values in parentheses are 95% confidence interval.*
[b]*Downgraded due to limitations of trial design.*
[c]*Downgraded due to inconsistency of results.*
[d]*Downgraded due to high probability of publication bias due to visual inspection of the funnel plot.*
[e]*Downgraded due to imprecision of results.*
[f]*Values in the SMD column are mean difference.*

DISCUSSION

Weight-loss interventions were effective for reducing pain, disability, and weight in people with knee and hip OA. We found small to moderate effects on pain intensity and disability from very low– and low-credibility evidence, compared to minimal care, in people with knee and hip OA. Weight-loss interventions were not more effective than exercise-only interventions for people with knee OA (low- and moderate-credibility evidence). Combined diet and exercise weight-loss interventions had small to moderate effects on pain intensity and disability, compared to either diet-only or exercise-only interventions, in people with knee OA (low- to moderate-credibility evidence), but these interventions were not more effective for weight loss. Weight-loss interventions had small to moderate effects on weight reduction in people with knee and hip OA (mean difference between 5.6 kg and 3.5 kg). Weight-loss interventions may not influence pain intensity, disability, or weight in people with spinal pain (very low–credibility evidence). While the pharmaceutical weight-loss approach appeared to produce large effects, based on the implausible standard deviation reported in that trial, the result is questionable.

Overweight and obesity have been attributed as a determinant of OA onset and progression.[44] Weight-loss interventions had small to moderate effects on core OA outcomes. Improvements from weight-loss interventions were equivalent to a 1-point difference on a 0-to-10 numeric rating scale and a 3.7-point difference on the 0-to-68 WOMAC function (disability) subscale. These effects are at the low end of clinically meaningful effect sizes.[19,49] Given the complex interventions included in our review, it is unclear whether the effects may be attributed to reduced weight or to other mechanisms (eg, self-efficacy, strength, or other cognitive constructs).

The effects observed for weight-loss interventions in our review are similar to or smaller than those of OA interventions that do not include weight-loss components. For example, advice and education and interventions aiming to promote OA self-management produce similar effect sizes to our findings.[32] Exercise interventions may have larger effects on pain and disability than weight-loss interventions.[20] While many people with OA are overweight,[8] comparisons of our results to those of reviews of other interventions should be undertaken with caution, due to the potentially different populations of trials that do not focus on weight-loss inter-

ventions (ie, those including nonoverweight individuals).[20]

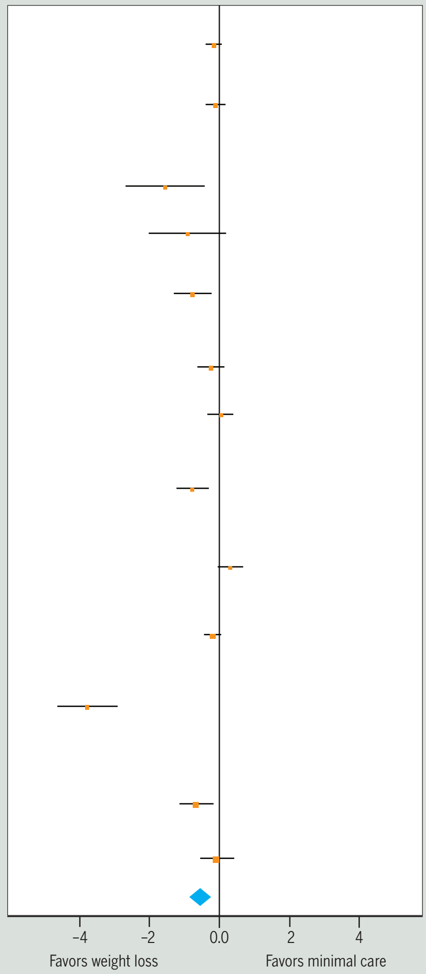
Strengths and Limitations in Relation to Other Studies

Our review was prospectively registered, conducted using best-practice Cochrane methods,[25] and reported according to the PRISMA guidelines.[51] We used a comprehensive search strategy, including trial registries. The scope of our review was wider than that of previous reviews in the field,[4,13,17] as it included 11 more trials and over 900 more participants. We also examined disability—an important outcome for people with OA and spinal pain that was omitted in previous reviews.[4,17] We calculated pooled intervention effects for a range of outcomes for specific conditions and conducted subgroup analysis by intervention type. Because the clinical interpretation of SMDs can be difficult, we re-expressed SMDs to provide effect estimates that can be more easily applied to clinical reasoning (**TABLE 2**).

We observed substantial statistical heterogeneity (I² greater than 50%) for some comparisons. We attempted to explore heterogeneity by subgroup analy-

Pain

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]					
Telephone coaching plus referral	−0.1613 ± 0.1157	151	149	9.3%	−0.16 (−0.39, 0.07)
Allen et al[2]					
Telephone coaching plus referral	−0.1101 ± 0.142	268	129	9.1%	−0.11 (−0.39, 0.17)
Ghroubi et al[23]					
Reduced-calorie diet plus exercise	−1.5539 ± 0.5795	12	6	4.4%	−1.55 (−2.69, −0.42)
Reduced-calorie diet	−0.9165 ± 0.5617	12	5	4.5%	−0.92 (−2.02, 0.18)
Lim et al[33]					
Exercise only	−0.7676 ± 0.2766	46	20	7.6%	−0.77 (−1.31, −0.23)
Messier et al[34]					
Reduced-calorie diet plus exercise	−0.2418 ± 0.1976	76	39	8.5%	−0.24 (−0.63, 0.15)
Reduced-calorie diet	0.04 ± 0.1945	82	39	8.6%	0.04 (−0.34, 0.42)
Miller et al[37]					
MR, reduced-calorie diet plus exercise	−0.7797 ± 0.242	39	35	8.0%	−0.78 (−1.25, −0.31)
O'Brien et al[41]					
Telephone coaching	0.3132 ± 0.1845	59	60	8.7%	0.31 (−0.05, 0.67)
Ravaud et al[43]					
Counseling plus education	−0.1897 ± 0.1196	146	181	9.3%	−0.19 (−0.42, 0.04)
Saraboon et al[50]					
Reduced-calorie diet plus exercise plus education	-3.7733 ± 0.4401	40	40	5.7%	-3.77 (−4.64, −2.91)
Somers et al[53]					
Reduced-calorie diet plus exercise plus PCS	−0.6855 ± 0.2396	62	26	8.1%	−0.69 (−1.16, −0.22)
Reduced-calorie diet plus exercise	−0.0861 ± 0.2387	59	25	8.1%	−0.09 (−0.55, 0.38)
Total[a]		1052	754	100.0%	−0.54 (−0.86, −0.22)



[a]*Heterogeneity: $\tau^2 = 0.27$, $\chi^2 = 95.97$, df = 12 (P<.0001), $I^2 = 87\%$. Test for overall effect: z = 3.31 (P = .0009).*
Abbreviations: IV, inverse variance; MR, meal replacement; PCS, pain coping skills; SE, standard error; SMD, standardized mean difference.

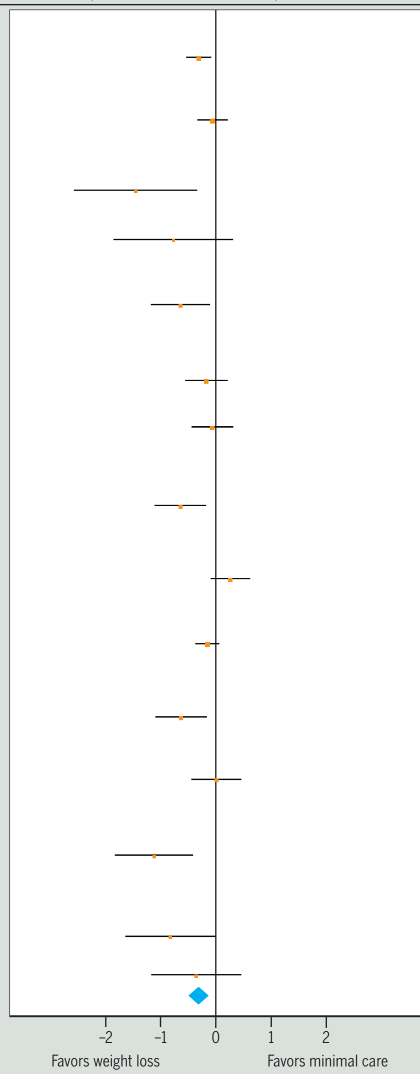
Figure continues on page 329.

FIGURE 3. Main meta-analyses of all weight-loss interventions versus minimal care for knee and hip OA for the outcomes of pain, disability, and weight. "Reduced-calorie diet plus exercise" is an intervention addressing weight loss via diet to reduce calorie intake, combined with an exercise program. The "MR" intervention addresses weight loss via diet using MRs, and the "education" intervention addresses weight loss via pain and condition-specific education. "Referral" is an intervention with specialist referral. Abbreviations: MR, meal replacement; OA, osteoarthritis.

sis based on intervention type, and downgraded the evidence credibility for inconsistency in GRADE assessments. We only found 3 trials of weight-loss interventions for spinal pain,[28,39,59] despite it being a leading cause of disability[22] with known impacts on co-occurring obesity.[52,57] We recommend caution when drawing conclusions from this limited number of trials with varied results, given the low credibility of evidence as assessed by GRADE and high heterogeneity for some analyses. We found few trials examining the impact of pharmacological weight-loss interventions overall (n = 3). We did not pool these trials due to differing comparison groups.[39,54,56] There were also no trials of other medical or surgical weight-loss interventions, and no trials reported on participants with hip OA

Disability

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]					
Telephone coaching plus referral	−0.3104 ± 0.1162	151	149	11.1%	−0.31 (−0.54, −0.08)
Allen et al[2]					
Telephone coaching plus referral	−0.0578 ± 0.1419	268	129	10.2%	−0.06 (−0.34, 0.22)
Ghroubi et al[23]					
Reduced-calorie diet plus exercise	−1.4544 ± 0.5703	12	6	2.1%	−1.45 (−2.57, −0.34)
Reduced-calorie diet	−0.7708 ± 0.5532	12	5	2.2%	−0.77 (−1.86, 0.31)
Lim et al[33]					
Exercise only	−0.6413 ± 0.274	46	20	6.0%	−0.64 (−1.18, −0.10)
Messier et al[34]					
Reduced-calorie diet plus exercise	−0.1732 ± 0.1973	76	39	8.2%	−0.17 (−0.56, 0.21)
Reduced-calorie diet	−0.062 ± 0.1946	82	39	8.3%	−0.06 (−0.44, 0.32)
Miller et al[37]					
MR, reduced-calorie diet plus exercise	−0.6445 ± 0.2391	39	35	6.9%	−0.64 (−1.11, −0.18)
O'Brien et al[41]					
Telephone coaching	0.2644 ± 0.1842	59	60	8.7%	0.26 (−0.10, 0.63)
Ravaud et al[43]					
Counseling plus education	−0.1543 ± 0.1127	146	181	11.2%	−0.15 (−0.38, 0.07)
Somers et al[53]					
Reduced-calorie diet plus exercise plus PCS	−0.6314 ± 0.2387	62	26	6.9%	−0.63 (−1.10, −0.16)
Reduced-calorie diet plus exercise	0.015 ± 0.2386	59	25	6.9%	0.01 (−0.45, 0.48)
Toda et al[56]					
Pharmacology plus MR	−1.122 ± 0.3622	22	15	4.2%	−1.12 (−1.83, −0.41)
Wolf et al[60]					
Reduced-calorie diet plus exercise	−0.8239 ± 0.4179	20	9	3.4%	−0.82 (−1.64, 0.00)
Reduced-calorie diet	−0.3599 ± 0.4186	21	8	3.4%	−0.36 (−1.18, 0.46)
Total[a]		1075	746	100.0%	−0.32 (−0.49, −0.14)



[a]*Heterogeneity: $\tau^2 = 0.06$, $\chi^2 = 33.30$, df = 14 (P = .003), $I^2 = 58\%$. Test for overall effect: z = 3.52 (P = .0004).*
Abbreviations: IV, inverse variance; MR, meal replacement; PCS, pain coping skills; SE, standard error; SMD, standardized mean difference.

Figure continues on page 330.

FIGURE 3 (CONTINUED). Main meta-analyses of all weight-loss interventions versus minimal care for knee and hip OA for the outcomes of pain, disability, and weight. "Reduced-calorie diet plus exercise" is an intervention addressing weight loss via diet to reduce calorie intake, combined with an exercise program. The "MR" intervention addresses weight loss via diet using MRs, and the "education" intervention addresses weight loss via pain and condition-specific education. "Referral" is an intervention with specialist referral. Abbreviations: MR, meal replacement; OA, osteoarthritis.

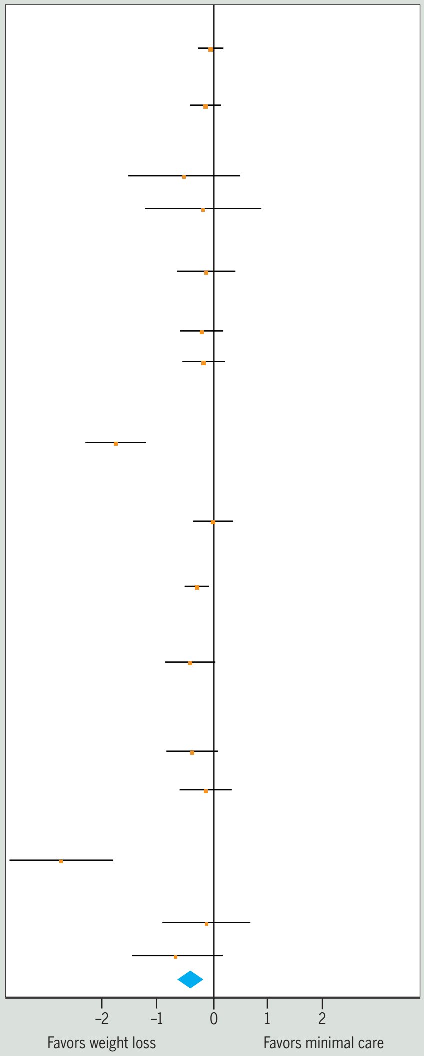
independent of knee OA. The subgroup analysis on the basis of intervention duration should be interpreted cautiously, because it did not account for intervention dose. Inconsistent information reported across trials precluded categorization by dose.

Implications for Practice and Policy

Current behavioral approaches might not consistently produce sufficient weight loss for meaningful effects on pain and disability.[9] Clinical practice guidelines suggest that people with overweight or obesity and OA require a weight loss of 5% to 7.5% of body weight for clinically meaningful improvements in pain and disability.[9,47] Behavioral approaches are recommended as the first line of care for weight loss.[47] We found that behavioral weight-loss interventions for knee and hip OA produced

Weight

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]					
Telephone coaching plus referral	−0.0564 ± 0.1155	151	149	8.7%	−0.06 (−0.28, 0.17)
Allen et al[2]					
Telephone coaching plus referral	−0.1526 ± 0.1421	268	129	8.3%	−0.15 (−0.43, 0.13)
Ghroubi et al[23]					
Reduced-calorie diet plus exercise	−0.5325 ± 0.51	12	6	3.4%	−0.53 (−1.53, 0.47)
Reduced-calorie diet	−0.1941 ± 0.5336	12	5	3.2%	−0.19 (−1.24, 0.85)
Lim et al[33]					
Exercise only	−0.1381 ± 0.2681	46	20	6.3%	−0.14 (−0.66, 0.39)
Messier et al[34]					
Reduced-calorie diet plus exercise	−0.2172 ± 0.1975	76	39	7.4%	−0.22 (−0.60, 0.17)
Reduced-calorie diet	−0.1844 ± 0.1949	82	39	7.5%	−0.18 (−0.57, 0.20)
Miller et al[37]					
MR, reduced-calorie diet plus exercise	−1.7559 ± 0.2786	40	33	6.1%	−1.76 (−2.30, −1.21)
O'Brien et al[41]					
Telephone coaching	−0.015 ± 0.1833	59	60	7.7%	−0.01 (−0.37, 0.34)
Ravaud et al[43]					
Counseling plus education	−0.3032 ± 0.1119	146	181	8.7%	−0.30 (−0.52, −0.08)
Saraboon et al[50]					
Reduced-calorie diet plus exercise plus education	−0.4221 ± 0.2291	40	40	6.9%	−0.42 (−0.87, 0.03)
Somers et al[53]					
Reduced-calorie diet plus exercise plus PCS	−0.3873 ± 0.2355	62	26	6.8%	−0.39 (−0.85, 0.07)
Reduced-calorie diet plus exercise	−0.145 ± 0.2389	59	25	6.8%	−0.14 (−0.61, 0.32)
Toda et al[56]					
Pharmacology plus MR	−2.7287 ± 0.4741	22	15	3.7%	−2.73 (−3.66, −1.80)
Wolf et al[60]					
Reduced-calorie diet plus exercise	−0.1344 ± 0.4018	20	9	4.4%	−0.13 (−0.92, 0.65)
Reduced-calorie diet	−0.6852 ± 0.4184	24	8	4.3%	−0.69 (−1.51, 0.13)
Total[a]		1119	784	100.0%	−0.42 (−0.64, −0.19)



[a]*Heterogeneity: τ^2 = 0.14, χ^2 = 64.30, df = 15 (P<.0001), I^2 = 77%. Test for overall effect: z = 3.58 (P = . 0003).*
Abbreviations: IV, inverse variance; MR, meal replacement; PCS, pain coping skills; SE, standard error; SMD, standardized mean difference.

FIGURE 3 (CONTINUED). Main meta-analyses of all weight-loss interventions versus minimal care for knee and hip OA for the outcomes of pain, disability, and weight. "Reduced-calorie diet plus exercise" is an intervention addressing weight loss via diet to reduce calorie intake, combined with an exercise program. The "MR" intervention addresses weight loss via diet using MRs, and the "education" intervention addresses weight loss via pain and condition-specific education. "Referral" is an intervention with specialist referral. Abbreviations: MR, meal replacement; OA, osteoarthritis.

weight loss between 3.5 and 5.6 kg. While our review supports weight loss as a generally effective treatment approach, behavioral interventions might not always be suitable as a first-line option, given their time-intensive nature, the resources they require, and their cost.

Although guidelines endorse weight loss as a core treatment for OA, our review suggests that exercise is a critical ingredient for managing OA. Weight loss might not contribute to greater effects on pain and disability. For example, we found that diet and exercise interventions led to greater improvements in pain and disability but no difference in weight loss. Causal mechanisms of weight-loss interventions may not be attributed to weight loss or changes to body mass index, but may be explained by other mediators.[48,58] Osteoarthritis management guidance should be cautious about overemphasizing the importance of weight loss for pain and disability, and instead focus on a comprehensive package of care, including exercise.

More research is needed to inform clinical practice decisions about weight loss for people with musculoskeletal conditions. Future research should focus on understanding whether weight loss is the mechanism of effect on pain and disability, and then how to maximize effects across the population. The 3 trials on pharmaceutical weight-loss interventions seem to report promising effects, but more research is needed to understand the effectiveness, safety, and applicability of these approaches. We identified an important evidence gap relating to spinal pain. As there is a high prevalence of overweight and obesity in people with spinal pain,[42,55] there is a need for more high-quality trials that investigate whether targeting weight loss is an important approach to care.

CONCLUSION

Compared to minimal care, weight-loss interventions reduced pain intensity and disability in people with knee and hip OA, but not in those with spinal pain. Weight-loss interventions were not more effective than exercise-only interventions for knee OA. There was limited evidence regarding the effect of weight-loss interventions for spinal pain. ◉

KEY POINTS

FINDINGS: There was low-credibility evidence that behavioral weight-loss interventions produced small to moderate improvements in pain intensity and disability in people with knee or hip osteoarthritis (OA) compared to minimal interventions. Weight-loss interventions were not more effective than exercise-only interventions for reducing pain or disability in people with knee OA. There was moderate-credibility evidence that combined diet and exercise weight-loss interventions improved pain intensity and disability compared to diet-only interventions for knee OA.

IMPLICATIONS: We found uncertainty in the evidence of effectiveness of weight-loss interventions for pain and disability in people with knee and hip OA. Guideline recommendations should be tempered to reflect uncertainty in effects of weight-loss interventions for pain intensity and disability. There was insufficient evidence of the effectiveness of pharmacological and other medical weight-loss interventions for patients with OA or spinal pain. More research is needed in these areas.

CAUTION: Most of the evidence was of low credibility and should be interpreted cautiously.

STUDY DETAILS

AUTHOR CONTRIBUTIONS: Drs Christopher Williams, John Wiggers, Serene Yoong, Luke Wolfenden, and Steven Kamper designed the review. Dr Christopher Williams, Emma Robson, and Debbie Booth developed the search strategy. Emma Robson and Drs Christopher Williams, Amanda Williams, Kate O'Brien, Rebecca Hodder, and Hopin Lee performed study selection and extracted data from included studies. Emma Robson and Drs Christopher Williams and Rebecca Hodder were involved in the data analysis. Emma Robson and Drs Christopher Williams, Steven Kamper, and Rebecca Hodder were involved in the interpretation and discussion of results. Emma Robson drafted the manuscript, and all authors revised it critically for important intellectual content and approved the final version of the article. All authors had access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr Christopher Williams is the guarantor.

DATA SHARING: All data relevant to the study are included in the article or are available as online appendices.

PATIENT AND PUBLIC INVOLVEMENT: There was no patient or public involvement in the completion of this study.

ACKNOWLEDGMENTS: *The authors thank information specialist Debbie Booth for assisting in the development and running of the search strategy.*

REFERENCES

1. Alghadir A, Anwer S, Brismée JM. The reliability and minimal detectable change of Timed Up and Go test in individuals with grade 1–3 knee osteoarthritis. *BMC Musculoskelet Disord*. 2015;16:174. https://doi.org/10.1186/s12891-015-0637-8
2. Allen KD, Oddone EZ, Coffman CJ, et al. Patient, provider, and combined interventions for managing osteoarthritis in primary care: a cluster randomized trial. *Ann Intern Med*. 2017;166:401-411. https://doi.org/10.7326/M16-1245
3. Allen KD, Yancy WS, Jr., Bosworth HB, et al. A combined patient and provider intervention for management of osteoarthritis in veterans: a randomized clinical trial. *Ann Intern Med*. 2016;164:73-83. https://doi.org/10.7326/M15-0378
4. Alrushud AS, Rushton AB, Kanavaki AM, Greig CA. Effect of physical activity and dietary restriction interventions on weight loss and the musculoskeletal function of overweight and obese older adults with knee osteoarthritis: a systematic review and mixed method data synthesis. *BMJ Open*. 2017;7:e014537. https://doi.org/10.1136/bmjopen-2016-014537
5. Altman R, Alarcón G, Appelrouth D, et al. The

American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis Rheum*. 1991;34:505-514. https://doi.org/10.1002/art.1780340502
6. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis Rheum*. 1986;29:1039-1049. https://doi.org/10.1002/art.1780290816
7. Aree-Ue S, Saraboon Y, Belza B. Long-term adherence and effectiveness of a multicomponent intervention for community-dwelling overweight Thai older adults with knee osteoarthritis: 1-year follow up. *J Gerontol Nurs*. 2017;43:40-48. https://doi.org/10.3928/00989134-20170111-09
8. Australian Institute of Health and Welfare. The Burden of Musculoskeletal Conditions in Australia: A Detailed Analysis of the Australian Burden of Disease Study 2011. Canberra, Australia: Australian Institute of Health and Welfare; 2017.
9. Bliddal H, Leeds AR, Christensen R. Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons – a scoping review. *Obes Rev*. 2014;15:578-586. https://doi.org/10.1111/obr.12173
10. Bliddal H, Leeds AR, Stigsgaard L, Astrup A, Christensen R. Weight loss as treatment for knee osteoarthritis symptoms in obese patients: 1-year results from a randomised controlled trial. *Ann Rheum Dis*. 2011;70:1798-1803. https://doi.org/10.1136/ard.2010.142018
11. Christensen P, Henriksen M, Bartels EM, et al. Long-term weight-loss maintenance in obese patients with knee osteoarthritis: a randomized trial. *Am J Clin Nutr*. 2017;106:755-763. https://doi.org/10.3945/ajcn.117.158543
12. Christensen R, Astrup A, Bliddal H. Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial. *Osteoarthritis Cartilage*. 2005;13:20-27. https://doi.org/10.1016/j.joca.2004.10.008
13. Christensen R, Bartels EM, Astrup A, Bliddal H. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis*. 2007;66:433-439. https://doi.org/10.1136/ard.2006.065904
14. Christensen R, Henriksen M, Leeds AR, et al. Effect of weight maintenance on symptoms of knee osteoarthritis in obese patients: a twelve-month randomized controlled trial. *Arthritis Care Res (Hoboken)*. 2015;67:640-650. https://doi.org/10.1002/acr.22504
15. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
16. Cohen SP. Epidemiology, diagnosis, and treatment of neck pain. *Mayo Clin Proc*. 2015;90:284-299. https://doi.org/10.1016/j.mayocp.2014.09.008
17. Cooper L, Ryan CG, Ells LJ, et al. Weight loss interventions for adults with overweight/obesity and chronic musculoskeletal pain: a mixed methods systematic review. *Obes Rev*. 2018;19:989-1007. https://doi.org/10.1111/obr.12686
18. Dobson F, Hinman RS, Roos EM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. *Osteoarthritis Cartilage*. 2013;21:1042-1052. https://doi.org/10.1016/j.joca.2013.05.002
19. Escobar A, Quintana JM, Bilbao A, Aróstegui I, Lafuente I, Vidaurreta I. Responsiveness and clinically important differences for the WOMAC and SF-36 after total knee replacement. *Osteoarthritis Cartilage*. 2007;15:273-280. https://doi.org/10.1016/j.joca.2006.09.001
20. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2015;1:CD004376. https://doi.org/10.1002/14651858.CD004376.pub3
21. Gay C, Eschalier B, Levyckyj C, Bonnin A, Coudeyre E. Motivators for and barriers to physical activity in people with knee osteoarthritis: a qualitative study. *Joint Bone Spine*. 2018;85:481-486. https://doi.org/10.1016/j.jbspin.2017.07.007
22. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1211-1259. https://doi.org/10.1016/S0140-6736(17)32154-2
23. Ghroubi S, Elleuch H, Kaffel N, Echikh T, Abid M, Elleuch MH. [Contribution of exercise and diet in the management of knee osteoarthritis in the obese]. *Ann Réadapt Méd Phys*. 2008;51:663-670. https://doi.org/10.1016/j.annrmp.2008.07.035
24. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64:383-394. https://doi.org/10.1016/j.jclinepi.2010.04.026
25. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Oxford, UK: The Cochrane Collaboration; 2011.
26. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557-560. https://doi.org/10.1136/bmj.327.7414.557
27. Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73:968-974. https://doi.org/10.1136/annrheumdis-2013-204428
28. Irandoust K, Taheri M, Shavikloo J. The effect of water-based aerobic training on the dynamic balance and walking speed of obese elderly men with low back pain. *Sleep Hypnosis*. 2018;20:233-240. https://doi.org/10.5350/Sleep.Hypn.2017.19.0155
29. Janke EA, Collins A, Kozak AT. Overview of the relationship between pain and obesity: what do we know? Where do we go next? *J Rehabil Res Dev*. 2007;44:245-262. https://doi.org/10.1682/jrrd.2006.06.0060
30. Juhl C, Lund H, Roos EM, Zhang W, Christensen R. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. *Arthritis*. 2012;2012:136245. https://doi.org/10.1155/2012/136245
31. Krismer M, van Tulder M, The Low Back Pain Group of the Bone and Joint Health Strategies for Europe Project. Low back pain (non-specific). *Best Pract Res Clin Rheumatol*. 2007;21:77-91. https://doi.org/10.1016/j.berh.2006.08.004
32. Kroon FP, van der Burg LR, Buchbinder R, Osborne RH, Johnston RV, Pitt V. Self-management education programmes for osteoarthritis. *Cochrane Database Syst Rev*. 2014:CD008963. https://doi.org/10.1002/14651858.CD008963.pub2
33. Lim JY, Tchai E, Jang SN. Effectiveness of aquatic exercise for obese patients with knee osteoarthritis: a randomized controlled trial. *PM R*. 2010;2:723-731. https://doi.org/10.1016/j.pmrj.2010.04.004
34. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum*. 2004;50:1501-1510. https://doi.org/10.1002/art.20256
35. Messier SP, Loeser RF, Mitchell MN, et al. Exercise and weight loss in obese older adults with knee osteoarthritis: a preliminary study. *J Am Geriatr Soc*. 2000;48:1062-1072. https://doi.org/10.1111/j.1532-5415.2000.tb04781.x
36. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA*. 2013;310:1263-1273. https://doi.org/10.1001/jama.2013.277669
37. Miller GD, Jenks MZ, Vendela M, Norris JL, Muday GK. Influence of weight loss, body composition, and lifestyle behaviors on plasma adipokines: a randomized weight loss trial in older men and women with symptomatic knee osteoarthritis. *J Obes*. 2012;2012:708505. https://doi.org/10.1155/2012/708505
38. Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring)*. 2006;14:1219-1230. https://doi.org/10.1038/oby.2006.139
39. Muehlbacher M, Nickel MK, Kettler C, et al. Topiramate in treatment of patients with chronic low back pain: a randomized, double-blind, placebo-controlled study. *Clin J Pain*. 2006;22:526-531. https://doi.org/10.1097/.ajp.0000192516.58578.a4
40. National Clinical Guideline Centre. Osteoarthritis: Care and Management in Adults. London, UK:

National Institute for Health and Care Excellence; 2014.

41. O'Brien KM, Wiggers J, Williams A, et al. Telephone-based weight loss support for patients with knee osteoarthritis: a pragmatic randomised controlled trial. *Osteoarthritis Cartilage*. 2018;26:485-494. https://doi.org/10.1016/j.joca.2018.01.003

42. Peng T, Pérez A, Pettee Gabriel K. The association among overweight, obesity, and low back pain in U.S. adults: a cross-sectional study of the 2015 National Health Interview Survey. *J Manipulative Physiol Ther*. 2018;41:294-303. https://doi.org/10.1016/j.jmpt.2017.10.005

43. Ravaud P, Flipo RM, Boutron I, et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *BMJ*. 2009;338:b421. https://doi.org/10.1136/bmj.b421

44. Reijman M, Pols HA, Bergink AP, et al. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip: the Rotterdam Study. *Ann Rheum Dis*. 2007;66:158-162. https://doi.org/10.1136/ard.2006.053538

45. Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol*. 2002;21:419-426. https://doi.org/10.1037//0278-6133.21.5.419

46. Riecke BF, Christensen R, Christensen P, et al. Comparing two low-energy diets for the treatment of knee osteoarthritis symptoms in obese patients: a pragmatic randomized clinical trial. *Osteoarthritis Cartilage*. 2010;18:746-754. https://doi.org/10.1016/j.joca.2010.02.012

47. Royal Australian College of General Practitioners. Guideline for the Management of Knee and Hip Osteoarthritis. East Melbourne, Australia: Royal Australian College of General Practitioners; 2018.

48. Runhaar J, Beavers DP, Miller GD, et al. Inflammatory cytokines mediate the effects of diet and exercise on pain and function in knee osteoarthritis independent of BMI. *Osteoarthritis Cartilage*. 2019;27:1118-1123. https://doi.org/10.1016/j.joca.2019.04.009

49. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain*. 2004;8:283-291. https://doi.org/10.1016/j.ejpain.2003.09.004

50. Saraboon Y, Aree-Ue S, Maruo SJ. The effect of multifactorial intervention programs on health behavior and symptom control among community-dwelling overweight older adults with knee osteoarthritis. *Orthop Nurs*. 2015;34:296-308. https://doi.org/10.1097/NOR.0000000000000180

51. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*. 2015;350:g7647. https://doi.org/10.1136/bmj.g7647

52. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. *Am J Epidemiol*. 2010;171:135-154. https://doi.org/10.1093/aje/kwp356

53. Somers TJ, Blumenthal JA, Guilak F, et al. Pain coping skills training and lifestyle behavioral weight management in patients with knee osteoarthritis: a randomized controlled study. *Pain*. 2012;153:1199-1209. https://doi.org/10.1016/j.pain.2012.02.023

54. Strebkova E, Alekseeva L. Effect of pharmacological and non-pharmacological therapy of obesity on the clinical manifestations of osteoarthritis [poster]. *Ann Rheum Dis*. 2017;76:968-969. https://doi.org/10.1136/annrheumdis-2017-eular.2819

55. Su CA, Kusin DJ, Li SQ, Ahn UM, Ahn NU. The association between body mass index and the prevalence, severity, and frequency of low back pain: data from the Osteoarthritis Initiative. *Spine (Phila Pa 1976)*. 2018;43:848-852. https://doi.org/10.1097/BRS.0000000000002601

56. Toda Y, Toda T, Takemura S, Wada T, Morimoto T, Ogawa R. Change in body fat, but not body weight or metabolic correlates of obesity, is related to symptomatic relief of obese patients with knee osteoarthritis after a weight control program. *J Rheumatol*. 1998;25:2181-2186.

57. Wai EK, Rodriguez S, Dagenais S, Hall H. Evidence-informed management of chronic low back pain with physical activity, smoking cessation, and weight loss. *Spine J*. 2008;8:195-202. https://doi.org/10.1016/j.spinee.2007.10.024

58. Williams A, Lee H, Kamper SJ, et al. Causal mechanisms of a healthy lifestyle intervention for patients with musculoskeletal pain who are overweight or obese. *Clin Rehabil*. 2019;33:1088-1097. https://doi.org/10.1177/0269215519831419

59. Williams A, Wiggers J, O'Brien KM, et al. Effectiveness of a healthy lifestyle intervention for chronic low back pain: a randomised controlled trial. *Pain*. 2018;159:1137-1146. https://doi.org/10.1097/j.pain.0000000000001198

60. Wolf S, Foley S, Budiman-Mak E, et al. Predictors of weight loss in overweight veterans with knee osteoarthritis who participated in a clinical trial. *J Rehabil Res Dev*. 2010;47:171-181. https://doi.org/10.1682/jrrd.2009.08.0136

61. Yázigi FG. *Knee osteoarthritis and obesity: effectiveness of PICO aquatic exercise program on symptoms, physical fitness and quality of life* [thesis]. Lisbon, Portugal: University of Lisbon; 2014.

62. Zhang W, Doherty M, Peat G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis*. 2010;69:483-489. https://doi.org/10.1136/ard.2009.113100

APPENDIX A

SEARCH STRATEGY FOR MEDLINE (1946 TO PRESENT, WITH DAILY UPDATE)

	Search Term	Results, n
1	exp Obesity/	156932
2	Overweight/	14845
3	Weight Gain/	24699
4	Weight Loss/	27223
5	obes*.tw.	181310
6	(overweight or over weight or overeat* or over eat* or adipos*).tw.	105247
7	Body Mass Index/	91314
8	(weight adj3 (cycl* or reduc* or los* or maint* or decreas* or watch* or control* or gain* or chang* or increas* or diet*)).tw.	170762
9	((body mass index or bmi) adj3 (reduc* or maint* or decreas* or watch* or control* or gain* or chang* or increas* or diet*)).tw.	19367
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	452475
11	randomized controlled trial.pt.	411368
12	clinical trial/	505061
13	controlled clinical trial/	91657
14	Random Allocation/	86193
15	Double-Blind Method/	134958
16	Single-Blind Method/	21352
17	Placebos/	33996
18	Research Design/	84189
19	intervention studies/	8237
20	evaluation studies/	211418
21	Comparative Study/	1739732
22	Longitudinal Studies/	96307
23	cross-over studies/	37207
24	trial.tw.	374824
25	latin square.tw.	3449
26	(time adj series).tw.	15487
27	(before adj2 after adj3 (stud* or trial* or design*)).tw.	9322
28	((singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)).tw.	133576
29	placebo*.tw.	162626
30	random*.tw.	716650
31	(matched adj (communit* or school* or population*)).tw.	1682
32	(comparison group* or control* group*).tw.	308309
33	matched pair*.tw.	6185
34	outcome stud*.tw.	5787
35	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34	3272989
36	exp Osteoarthritis/	47218
37	exp Back Pain/	30960
38	Neck Pain/	4989
39	(backache or neckache).tw.	1951
40	exp Musculoskeletal Pain/	1690
41	Sciatica/	4419
42	Neuralgia/	9417
43	(dorsalgia or cervicalgia).tw.	124
44	((Cervical Vertebrae or back or knee* or neck or spin* or hip* or lumb* or joint* or musculoske*) adj3 (pain* or ache* or aching or complaint* or stiff* or dysfunction* or disabil* or trauma* or disorder* or injur*)).tw.	127932

Table continues on B2.

APPENDIX A

	Search Term	Results, n
45	(osteoarthr* or osteo arthr*).tw.	43713
46	Coxarthr*.tw.	1597
47	36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	205106
48	10 and 35 and 47	1478
49	(animals not (humans and animals)).sh.	4022024
50	48 not 49	1383

APPENDIX B

INTERVENTION DETAILS OF INCLUDED TRIALS

Study/Type/Country/Trial	Condition/BMI/Arms	Intervention Group (Label Provided)/Duration, Content	Comparison Group (Label Provided)/Content	Length of Follow-up/Lost to Follow-up/Intervention Adherence	Primary/Secondary Outcomes
Allen et al[3] C-RCT United States	Knee/hip OA (n = 300) >25 kg/m^2 2 arms	Multifocused with weight loss (n = 151; telephone coaching for weight loss and primary care provider referrals) 12 mo. Patients received telephone counseling calls for weight management, physical activity, and cognitive behavioral strategies for managing pain. Primary care providers were trained to consider an algorithm-based referral method for OA treatments such as MOVE!, knee braces, injections, etc	Minimal care (n = 149; usual care) No description provided	12 mo 9% NR	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) BMI, mental health (PHQ), physical activity (CHAMPS)
Allen et al[2] C-RCT United States	Knee and/or hip OA (n = 537) >25 kg/m^2 4 arms	Multifocused with weight loss (n = 128; telephone weight management) 12 mo. Patients received telephone calls for weight management, physical activity, and cognitive behavioral strategies for managing pain Multifocused with weight loss (n = 140; telephone coaching for weight loss and primary care provider referrals) 12 mo. Combined patient and provider intervention	Minimal care (n = 129; usual care) No description provided	12 mo 19.1% Patients, 43%; providers, 47% of calls completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) BMI, mental health (PHQ), physical activity (CHAMPS)
Bliddal et al,[10] Christensen et al[12] RCT Denmark	Knee OA (n = 96) >28 kg/m^2 2 arms	Weight loss focused (n = 48; meal replacements and reduced-calorie diet) 12 mo. First 8 wk: meal replacement formula diet providing 810 kcal/d. In weeks 8-32, participants received weekly or second weekly nutrition sessions to achieve a 1200-kcal/d intake for weight loss. In weeks 32-36, patients used original meal replacements, and in weeks 36-52 nutrition sessions	Weight loss focused (n = 48; reduced-calorie diet) 2-h nutrition presentation at weeks 0, 8, 32, 36, and 52 to try to achieve caloric restriction of 1200 kcal/d	12 mo 41.7% 58% completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms)
Christensen et al[11] RCT Denmark LIGHT	Knee OA (n = 153) >30 kg/m^2 2 arms	Weight loss focused (n = 76; meal replacements and diet modification) 3 y. Three 5-wk weight-loss periods of consuming meal replacement products (totaling an intake of 810 kcal/d) and attending dietitian sessions for weight loss and maintenance advice. Participants were instructed to eat 1200 kcal/d between the 5-wk weight-loss periods	Weight loss focused (n = 77; meal replacements) 1-2 meal replacement products daily to reduce caloric intake. Group dietitian sessions 3 times weekly	3 y 29.5% 70% of sessions completed	Pain (KOOS pain subscale) and disability (KOOS function in sport and recreation subscale) Weight (kilograms), KOOS knee-related QoL subscale
Ghroubi et al[23] RCT France	Knee OA (n = 56) >30 kg/m^2 4 arms	Weight loss focused (n = 14; reduced-calorie diet) 8 wk. Diet prescription with 25%-30% reduction in calories Weight loss focused (n = 15; reduced-calorie diet and exercise) 8 wk. Dietary weight loss and exercise interventions combined	Minimal care (n = 14; control) Description not provided Exercise only (n = 13; exercise program) Aerobic and strength exercise for 60 min, 3 times per week	8 wk 19.7% NR	Pain (VAS) and disability (WOMAC) Weight (kilograms), physical performance (6MW)
Irandoust et al[28] RCT Iran	LBP (n = 36) NR 2 arms	Weight loss focused (n = 18; aquatic exercise program and diet modification) 4 mo. Water-based training for 60 min, 3 times per week. Diet adjusted based on calorie recommendations from nutritionist	Minimal care (n = 18; control) Description not provided	4 mo NR NR	Pain (VAS) Weight (kilograms)

Table continues on B4.

APPENDIX B

Study/Type/Country/Trial	Condition/BMI/Arms	Intervention Group (Label Provided)/Duration, Content	Comparison Group (Label Provided)/Content	Length of Follow-up/Lost to Follow-up/Intervention Adherence	Primary/Secondary Outcomes
Lim et al[33] RCT the Netherlands	Knee OA (n = 75) >25 kg/m^2 3 arms	Weight loss focused (n = 26; aquatic exercise program) 8 wk. Aquatic gym program for 40 min, 3 times per week Weight loss focused (n = 25; land-based exercise program) 8 wk. Land-based gym conditioning program for 40 min, 3 times per week	Minimal care (n = 24; home-based exercise) Advice for home-based exercise	8 wk 12% Aquatic, 92%; land, 88% of sessions completed	Pain (BPI, 0-11) and disability (WOMAC) Weight (kilograms), mental health (SF-36 MCS)
Messier et al[35] RCT United States	Knee OA (n = 24) >28 kg/m^2 2 arms	Weight loss focused (n = 13; reduced-calorie diet and exercise) 6 mo. Weekly 60-min nutrition classes for weight loss and an exercise program for 60 min, 3 times per week	Exercise only (n = 11; exercise program) Exercise program for 60 min, 3 times per week	6 mo 12.5% Diet plus exercise, 95% of sessions completed	Pain (knee pain scale, ambulation intensity of 0-6) and disability (FAST Functional Performance Inventory) Weight (kilograms), physical performance (6MW)
Messier et al,[34] Rejeski et al[45] RCT United States ADAPT	Knee OA (n = 316) >28 kg/m^2 4 arms	Weight loss focused (n = 82; reduced-calorie diet) 18 mo. 3-phase weight-loss program with weekly individual and group dietitian sessions, and phone counseling for weight loss. Goals were to produce and maintain an average weight loss of 5% Weight loss focused (n = 76; reduced-calorie diet and exercise) 18 mo. Dietary weight loss and exercise interventions combined	Minimal care (n = 78; healthy lifestyle education) Monthly 1-h meetings and calls for topics on OA, recommendations for exercise and weight Exercise only (n = 80; exercise program) Exercise program for 60 min, 3 times per week; facility-based transition or home based. Telephone contact	18 mo 20.3% Diet, 72%; exercise, 60%; diet plus exercise, 64% of sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW), mental health (SF-36 MCS)
Messier et al[36] RCT United States IDEA	Knee OA (n = 454) >27-41 kg/m^2 3 arms	Weight loss focused (n = 150; meal replacements and reduced-calorie diet) 18 mo. 2 meal replacement shakes per day and a calorie-controlled third meal. The diet plan provided for 1200 kcal/d. Participants also attended weekly nutrition education sessions Weight loss focused (n = 152; meal replacements, reduced-calorie diet, and exercise) 18 mo. Diet plus exercise intervention combined	Exercise only (n = 152; exercise program) Exercise program for 60 min, 3 times per week. Facility, then home based, and telephone contact	18 mo 12.2% Diet, 61%; diet plus exercise, 63% of sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW), mental health (SF-36 MCS)
Miller et al [37,38] RCT United States	Knee OA (n = 87) >30 kg/m^2 2 arms	Weight loss focused (n = 44; meal replacements, reduced-calorie diet, and exercise) 6 mo. Partial meal replacements, nutrition education, and behavioral and educational sessions. Dietary energy was 4600 kJ/d for women and 5022 kJ/d for men. Participants also attended exercise sessions in groups of 6-12, for 60 min, 3 times per week	Minimal care (n = 43; weight stable) Bimonthly meetings on OA general health and weight-maintenance content	6 mo 9.2% Intervention group, 77% of exercise and 75% of nutrition sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (kilograms), physical performance (6MW)
Muehlbacher et al[39] RCT Germany	CLBP (n = 96) NR 2 arms	Weight loss focused (n = 48; pharmaceutical) 10 wk. Blinded medication of 50-mg topiramate titrated at 50 mg/wk to a dose of 200 mg/d in the sixth week, remaining constant	Minimal care (n = 48; placebo) Participants took blinded placebo drug	10 wk 8.4% NR	Pain (PRI of the MPQ, 0-40) and disability (ODQ) Weight (kilograms), mental health (SF-36 MCS)

Table continues on B5.

APPENDIX B

Study/Type/ Country/Trial	Condition/BMI/ Arms	Intervention Group (Label Provided)/Duration, Content	Comparison Group (Label Provided)/Content	Length of Follow-up/Lost to Follow-up/Intervention Adherence	Primary/Secondary Outcomes
O'Brien et al[41] RCT Australia	Knee OA (n = 120) 27-40 kg/m^2 2 arms	Weight loss focused (n = 60; telephone coaching for weight loss) 6 mo. Brief advice and referral to free telephone-based weight-loss coaching service	Minimal care (n = 60; usual care) Description not provided	6 mo 12% 34% completed ≥6 calls	Pain (NRS, 0-10) and disability (WOMAC function subscale) Weight (kilograms), mental health (SF-12 Version 2 MCS), physical activity (MVPA), dietary intake (FFQ)
Ravaud et al[43] C-RCT France ARTIST	Knee OA (n = 336) 25-35 kg/m^2 2 arms	Multifocused with weight loss (n = 154; goal-oriented OA consultations and weight-loss advice) 30 d. 3 goal-oriented rheumatologist visits. Each visit focused on 1 topic; the first visit provided OA education and advice and the next 2 visits focused on an exercise regime and weight loss, with tailored counseling	Minimal care (n = 182; usual care) 3 usual-care visits to rheumatologist	4 mo 12.3% 95% attended 3 consultations	Pain (NRS, 0-10) and disability (WOMAC function subscale) Weight (kilograms), mental health (SF-12 MCS)
Riecke et al[46] RCT (phase 1 of 2) Christensen et al[14] RCT (phase 2 of 2) Denmark	Phases 1 and 2: knee OA (n = 192) NR Phase 1, 2 arms; phase 2, 3 arms	Phase 1: weight loss focused (n = 96; meal replacements and reduced-calorie diet) 16 wk. 8 wk of a 415-kcal/d diet, followed by 8 wk of a hypoenergetic diet of normal foods, restricted to 1200 kcal/d. Patients attended 1.5-h weekly nutrition sessions to reinforce and encourage compliance Phase 2: weight loss focused (n = 64; meal replacements and reduced-calorie diet) 52 wk. Focus was on long-term lifestyle modifications to reach weight-loss goals. Weekly 60-min sessions where patients were provided with enough meal replacement formula products for 1 per day	Phase 1: weight loss focused (n = 96; meal replacements and reduced-calorie diet) Meal replacement formula: 810 kcal/wk for 8 wk and same hypoenergetic diet and nutrition sessions as the intervention group Phase 2: minimal care (n = 64; usual care) No attention provided Phase 2: exercise only (n = 64; exercise program) Participants completed 60-min exercise sessions 3 d/wk	68 wk 12.7% 90% of sessions completed	Pain (OMERACT-OARSI VAS, 0-100) and disability (OMERACT-OARSI VAS, 0-100) Weight (kilograms), mental health (SF-36 MCS), KOOS knee-related QoL subscale
Aree-Ue et al,[7] Saraboon et al[50] C-RCT Thailand	Knee OA (n = 80) 23-29 kg/m^2 2 arms	Multifocused with weight loss (n = 40; OA education, reduced-calorie diet, and exercise) 8 wk. 2-h workshops, 3 delivered in 1 wk. Education on knee OA and weight-reduction program, including information on food selection and an exercise regime. Home visits conducted at weeks 2, 4, and 6 following the workshops to support participants in healthy behavior change	Minimal care (n = 40; control) Booklet and DVD on OA	8 wk NR NR	Pain (NRS, 0-10) Weight (kilograms), physical performance (TUG)
Somers et al[53] RCT United States	Knee OA (n = 232) 25-42 kg/m^2 4 arms	Weight loss focused (n = 59; reduced-calorie diet and exercise) 24 wk. 16 weekly sessions of the LEARN program for weight management and appetite-awareness training. Goal was to lose 0.45-0.92 kg/wk using a 1200-kcal/d or 1500-kcal/d diet. Participants also attended group exercise sessions for 90 min, 3 times a week Multifocused with weight loss (n = 62; PCST reduced-calorie diet, and exercise) 24 wk. Behavior, weight-loss diet, and exercise program and PCST content combined	Minimal care (n = 51; control) No attention provided	PTA, 24 wk plus 6 mo plus 12 mo 29.75% BWM, 65%; PCST plus BWM, 73% of sessions completed	Pain (WOMAC pain subscale) and disability (WOMAC function subscale) Weight (pounds), mental health (AIMS psychological scale)

Table continues on B6.

APPENDIX B

Study/Type/Country/Trial	Condition/BMI/Arms	Intervention Group (Label Provided)/Duration, Content	Comparison Group (Label Provided)/Content	Length of Follow-up/Lost to Follow-up/Intervention Adherence	Primary/Secondary Outcomes
Strebkova and Alekseeva[54] RCT Russia	Knee OA (n = 50) >30 kg/m^2 2 arms	Weight loss focused (n = 25; pharmaceuticals, reduced-calorie diet, and exercise) 6 mo. Dose of orlistat: 120 mg, 3 times per day during meals, and hypocaloric diet with deficit of 500-600 kcal for weight loss. Explanations provided for exercises	Weight loss focused (n = 25; reduced-calorie diet and exercise) Hypocaloric diet with deficit of 500-600 kcal and explanations for exercises	6 mo 0% 100% drug compliance	Pain (WOMAC pain VAS, 0-100) and disability (WOMAC function VAS, 0-100) Weight (kilograms)
Toda et al[56] RCT Japan	Knee OA (n = 40) >26.4 kg/m^2 2 arms	Weight loss focused (n = 22; pharmaceuticals and exercise) 6 wk. Participants took mazindol (Sanorex; Sandoz-Wander) once per day to restrict appetite; meal replacements and basic exercise instructions (30 min/d)	Minimal care (n = 18; brief exercise instruction) Exercise instruction and NSAIDs twice per day	6 wk 7.5% NR	Disability (Lequesne index of severity) Weight (kilograms), physical activity (steps per day)
Williams et al[59] RCT Australia	CLBP (n = 160) 27-40 kg/m^2 2 arms	Multifocused with weight loss (n = 79; CLBP education and telephone coaching for weight loss) 6 mo. Brief advice over the phone and 1 physical therapy clinical consultation providing back pain education. All patients referred to telephone-based weight-loss coaching service	Minimal care (n = 80; usual care) Description not provided	26 wk 21.8% 41% completed ≥6 calls	Pain (NRS, 0-10) and disability (RMDQ) Weight (kilograms), mental health (SF-12 Version 2 MCS), physical activity (MVPA), dietary intake (FFQ)
Wolf et al[60] RCT United States	Knee OA (n = 110) NR 4 arms	Weight loss focused (n = 27; reduced-calorie diet) 24 wk. Food diary completion and attending 16 × 60-min weekly dietitian-run sessions of the LEARN program for weight management, and then biweekly 60-min sessions for 8 wk Weight loss focused (n = 28; reduced-calorie diet and exercise) 24 wk. Diet and exercise intervention combined	Minimal care (n = 25; usual care) 16 weekly sessions and 8 biweekly sessions with trial staff, discussing health-related issues, medications, etc. No nutrition or exercise advice Exercise (n = 30; exercise program) Weekly home-based exercise program of 60-min sessions for 16 wk and biweekly for 8 wk	24 wk 22% NR	Disability (WOMAC function subscale) Weight (pounds), physical performance (6MW), mental health (SF-36 MCS)
Yázigi[61] RCT Portugal	Knee OA (n = 52) NR 2 arms	Weight loss focused (n = 26; aquatic exercise program) 12 wk. Aquatic exercise program for 60 min, 2 times per week	Weight management program (n = 26) PESO educational program to prevent obesity and manage weight and health	12 wk 7.7% NR	Pain (BPI) and disability (KOOS) Weight (kilograms), KOOS knee-related QoL subscale

Abbreviations: 6MW, 6-minute walk; ADAPT, Arthritis, Diet, and Activity Promotion Trial; AIMS, Arthritis Impact Measurement Scales; ARTIST, osteoarthritis intervention standardized; BMI, body mass index; BPI, Brief Pain Inventory; BWM, behavioral weight management; CHAMPS, Community Healthy Activities Model Program for Seniors; CLBP, chronic low back pain; C-RCT, cluster randomized controlled trial; FFQ, Food Frequency Questionnaire; IDEA, Intensive Diet and Exercise for Arthritis; KOOS, Knee injury and Osteoarthritis Outcome Score; LBP, low back pain; LEARN, Lifestyle, Exercise, Attitudes, Relationships, Nutrition; LIGHT, Long-term Intervention With Weight Loss in Patients With Concomitant Obesity and Knee Osteoarthritis; MCS, mental component summary; MPQ, McGill Pain Questionnaire; MVPA, moderate to vigorous physical activity; NR, not reported; NRS, numeric rating scale; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; OARSI, Osteoarthritis Research Society International; ODQ, Oswestry Low Back Pain Disability Questionnaire; OMERACT, Outcome Measures in Rheumatology; PCST, pain coping skills training; PHQ, Patient Health Questionnaire; PRI, Pain Rating Index; PTA, posttreatment average; QoL, quality of life; RCT, randomized controlled trial; RMDQ, Roland-Morris Disability Questionnaire; SF-12, Medical Outcomes Study 12-Item Short-Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; TUG, timed up and go; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

APPENDIX B

RESULTS OF TRIALS NOT INCLUDED IN META-ANALYSES[a]

Study/ Comparators	Reason Not in MA	Pain	Disability	Weight	Performance/ Activity	Mental Health	QoL	Dietary Outcomes
Bliddal et al[10] n = 96 LED versus conventional diet	Active weight-loss control group could not be synthesized into comparison groups	WOMAC pain subscale: MD, 7.2 (95% CI: 1, 13.4); *P* = .02	WOMAC function subscale: MD, 3.7 (95% CI: −1.9, 9.2); *P* = .20	MD, 7.3 kg (95% CI: 5, 10); *P*≤.01	NR	NR	NR	NR
Christensen et al[11] n = 153 Intermittent diet versus regular diet	Active weight-loss control group unable to be synthesized into comparison groups	KOOS pain subscale: MD, 0.3 (95% CI: −4.4, 5.0); *P* = .91	KOOS function subscale: MD, 0.1 (95% CI: −5.5, 5.2); *P* = .97	MD, 1.06 kg (95% CI: 0.63, 2.75); *P* = .22	NR	NR	KOOS QoL subscale: MD, 0.8 (95% CI: −4.3, 5.8); *P* = .77	NR
Irandoust et al[28] n = 36 Aquatic exercise plus diet versus control	Primary outcome data not sufficient to be included in MA	Pain VAS: *P* = .001	NR	Follow-up: aquatic exercise plus diet, 80.9 to 79.2 kg; control, 83.5 to 79.5 kg; *P*<.001	TUG: mean change for aquatic exercise plus diet, 1.85 ± 0.004; *P* = .001; control, 1.92 ± 0.03; *P* = .958	NR	NR	NR
Miller et al[38] n = 87 Weight loss versus weight stable	Lack of dietary data to synthesize	In MA	In MA	In MA	In MA	NR	NR	Energy intake: weight loss, 1396 ± 64 cal; weight stable, 1817 ± 71 cal
O'Brien et al[41] n = 120 Telephone weight loss versus usual care	Lack of dietary data to synthesize	In MA	In MA	In MA	In MA	In MA	NR	Fruit intake OR = 0.85 (95% CI: 0.38, 1.89); vegetable intake OR = 0.35 (95% CI: 0.16, 0.77); consumption of DC more than once per week OR = 0.36 (95% CI: 0.08, 1.55)
Ravaud et al[43] n = 336 Standard consultation versus usual care	Postintervention results in MA; long-term results presented here	Standard consultations, −1.35 ± 2.48; usual care, −0.86 ± 2.59	Standard consultations, −8.67 ± 12.05; usual care, −5.44 ± 12.97	Standard consultations, −2.85 ± 4.76; usual care, −2.07 ± 4.37; *P* = .005	Standard consultations, 0.23 ± 0.72; usual care, 0.08 ± 0.85	NR	NR	NR

Table continues on B8.

APPENDIX B

Study/ Comparators	Reason Not in MA	Pain	Disability	Weight	Performance/ Activity	Mental Health	QoL	Dietary Outcomes
Riecke et al[46] n = 192 Phase 1: VLED versus LED Christensen et al[14] n = 192 Phase 2: diet versus exercise versus control	A 2-phase RCT; the active weight-loss control group was unable to be synthesized into comparison groups	Phase 1: OMERACT-OARSI pain MD, 1.1 (95% CI: –4.11, 6.32) Phase 2: pain VAS mean change for diet, –6.1 (95% CI: –11.1, –1.1); exercise, –5.6 (95% CI: –10.5, –0.6); control, –5.5 (95% CI: –10.5, –0.5); *P* = .98	Phase 1: OMERACT-OARSI disability MD, 1.69 (95% CI: –4.16, 7.54) Phase 2: disability VAS mean change for diet, –7.5 (95% CI: –12.8, –2.1); exercise, –7.6 (95% CI: –13, –2.2); control, –9 (95% CI: –14.4, –3.6); *P* = .91	Phase 1: MD, 1.08 kg (95% CI: –0.67, 2.81) Phase 2: mean change for diet, –10.96 kg (95% CI: –12.83, –9.09); exercise, –6.24 kg (95% CI: –8.11, –4.38); control, –8.23 kg (95% CI: –10.09, –6.36); *P* = .002	Phase 2: 6MW mean change for diet, 37.5 (95% CI: 22.8, 52.3); exercise, 38.5 (95% CI: 23.7, 53.2); control, 22.9 (95% CI: 7.9, 37.9); *P* = .3	Phase 1: SF-36 MCS MD, –3.11 (95% CI: –5.49, –0.73) Phase 2: SF-36 MCS mean change for diet, –0.3 (95% CI: –2.1, 1.6); exercise, 0.1 (95% CI: –1.7, 2); control, 1.3 (95% CI: –0.5, 3.2); *P* = .5	Phase 2: KOOS QoL subscale mean change for diet, 8.2 (95% CI: 4.5, 11.9); exercise, 5.8 (95% CI: 2.1, 9.5); control, 5.4 (95% CI: 1.7, 9.2); *P* = .5	NR
Saraboon et al[50] n = 80 MUFIP versus control	Postintervention results in MA; long-term results presented here	VAS: MUFIP, 1.1 ± 1; control, 4.2 ± 2.7; ES, 0.24	NR	MUFIP, 61.1 ± 9.6 kg; control, 64.3 ± 9.5 kg	TUG: MUFIP, 9 ± 1.7; control, 13.3 ± 2.9; ES, 0.21	NR	NR	NR
Strebkova and Alekseeva[54] n = 50 Orlistat versus diet plus PA	Active weight-loss control group unable to be synthesized into comparison groups	WOMAC pain subscale: orlistat change, –118 ± 96.4; diet plus PA, –48 ± 74.1	WOMAC function subscale: orlistat change, –415.9 ± 322.14; diet plus PA, –160.7 ± 354.4	Orlistat change, –10.5 ± 11.37 kg; diet plus PA, –0.9 ± 17.4 kg	NR	NR	NR	NR
Toda et al[56] n = 6 Weight loss versus control	Unable to use follow-up data in MA, as change data were required	NR	NR	NR	Steps per day (10³): weight loss, 7.5 ± 1.7; control, 7.3 ± 2.1	NR	NR	NR
Williams et al[59] n = 160 Telephone weight-loss coaching versus usual care	Lack of PA and dietary data to synthesize	NR	NR	NR	Minutes of MVPA per week: MD, 99.3 (95% CI: –260.2, 61.5)	NR	NR	Fruit intake OR = 0.79 (95% CI: 0.38, 1.63), vegetable intake OR = 1.3 (95% CI: 0.62, 2.72), consumption of DC more than once per week OR = 1.11 (95% CI: 0.36, 2.72)
Yázigi[61] n = 52 AQE versus PESO	Active weight-loss control group unable to be synthesized into comparison groups	KOOS pain subscale: AQE, 69.6 ± 19; PESO, 53.7 ± 19; *P*≤.001	KOOS function subscale: AQE, 52.2 ± 25; PESO, 36.5 ± 27; *P*≤.001	Body mass: AQE, 87.3 ± 11; PESO, 92.8 ± 16.8; *P* = .006	6MW: AQE, 18 ± 42; PESO, 55 ± 38; *P*≤.001	BDI: AQE, 6.2 ± 7; PESO, 11.1 ± 8; *P*≤.05	KOOS QoL subscale: AQE, 48.3 ± 25; PESO, 39.9 ± 21; *P*≤.05	NR

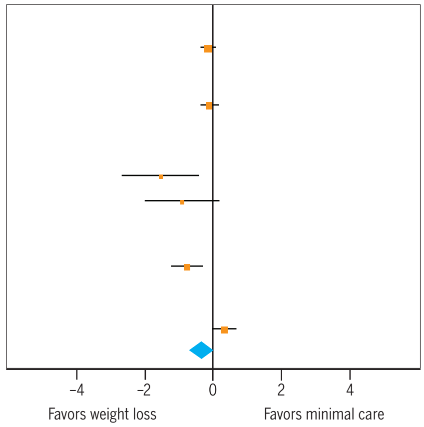
Abbreviations: 6MW, 6-minute walk; AQE, aquatic exercise; BDI, Beck Depression Inventory; CI, confidence interval; DC, discretionary choices; ES, effect size; KOOS, Knee injury and Osteoarthritis Outcome Score; LED, low-energy diet; MA, meta-analysis; MCS, mental component summary; MD, mean difference; MUFIP, multifactorial intervention program; MVPA, moderate to vigorous physical activity; NR, not reported; OARSI, Osteoarthritis Research Society International; OMERACT, Outcome Measures in Rheumatology; OR, odds ratio; PA, physical activity; QoL, quality of life; RCT, randomized controlled trial; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; TUG, timed up and go; VAS, visual analog scale; VLED, very low–energy diet; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[a]*Values are mean ± SD unless otherwise indicated.*

APPENDIX C

SENSITIVITY ANALYSIS: META-ANALYSIS RESULTS FOR ALL PRIMARY OUTCOMES AND WEIGHT FOR 2 COMPARISONS, EXCLUDING HIGH-RISK-OF-BIAS STUDIES

Pain

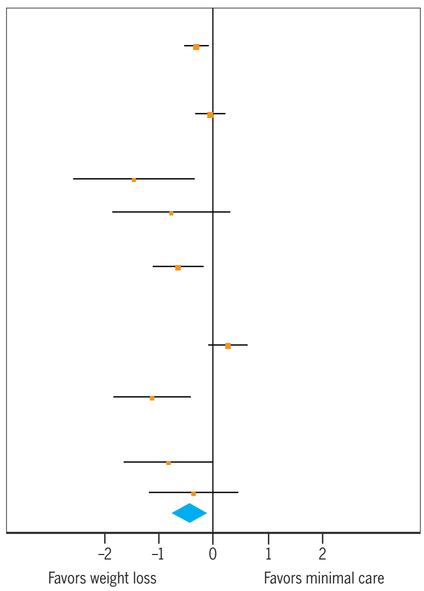
Study/Subgroup	SMD ± SE	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]			
Telephone coaching plus referral	−0.1613 ± 0.1157	23.8%	−0.16 (−0.39, 0.07)
Allen et al[2]			
Telephone coaching plus referral	−0.1101 ± 0.142	22.7%	−0.11 (−0.39, 0.17)
Ghroubi et al[23]			
Reduced-calorie diet plus exercise	−1.5539 ± 0.5795	7.2%	−1.55 (−2.69, −0.42)
Reduced-calorie diet	−0.9165 ± 0.5617	7.5%	−0.92 (−2.02, 0.18)
Miller et al[37]			
MR, reduced-calorie diet plus exercise	−0.7797 ± 0.242	18.0%	−0.78 (−1.25, −0.31)
O'Brien et al[41]			
Telephone coaching	0.3132 ± 0.1845	20.7%	0.31 (−0.05, 0.67)
Total[a]		100.0%	−0.32 (−0.68, 0.04)



[a]*Heterogeneity: τ^2 = 0.13, χ^2 = 20.85, df = 5 (P = .0009), I^2 = 76%. Test for overall effect: z = 1.75 (P = .08).*
Abbreviations: IV, inverse variance; MR, meal replacement; SE, standard error; SMD, standardized mean difference.

Disability

Study/Subgroup	SMD ± SE	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]			
Telephone coaching plus referral	−0.3104 ± 0.1162	17.8%	−0.31 (−0.54, −0.08)
Allen et al[2]			
Telephone coaching plus referral	−0.0578 ± 0.1419	17.0%	−0.06 (−0.34, 0.22)
Ghroubi et al[23]			
Reduced-calorie diet plus exercise	−1.4544 ± 0.5703	5.3%	−1.45 (−2.57, −0.34)
Reduced-calorie diet	−0.7708 ± 0.5532	5.6%	−0.77 (−1.86, 0.31)
Miller et al[37]			
MR, reduced-calorie diet plus exercise	−0.6445 ± 0.2391	13.4%	−0.64 (−1.11, −0.18)
O'Brien et al[41]			
Telephone coaching	0.2644 ± 0.1842	15.4%	0.26 (−0.10, 0.63)
Toda et al[56]			
Pharmacology plus MR	−1.122 ± 0.3622	9.4%	−1.12 (−1.83,−0.41)
Wolf et al[60]			
Reduced-calorie diet plus exercise	−0.8239 ± 0.4179	8.0%	−0.82 (−1.64, 0.00)
Reduced-calorie diet	−0.3599 ± 0.4186	8.0%	−0.36 (−1.18, 0.46)
Total[a]		100.0%	−0.43 (−0.73, −0.13)



[a]*Heterogeneity: τ^2 = 0.12, χ^2 = 25.69, df = 8 (P = .001), I^2 = 69%. Test for overall effect: z = 2.81 (P = .005).*
Abbreviations: IV, inverse variance; MR, meal replacement; SE, standard error; SMD, standardized mean difference.

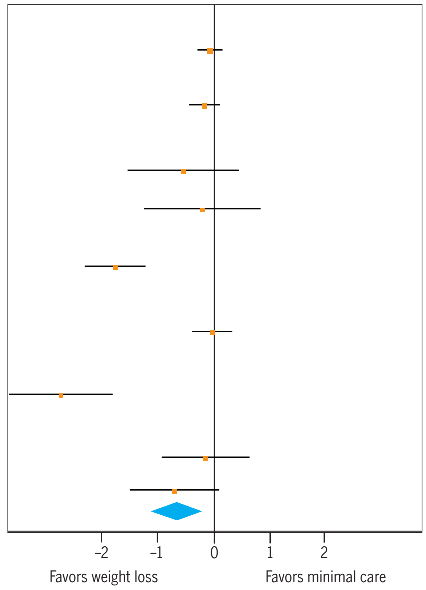
Figure continues on page B10.

FIGURE 1. Weight-loss interventions versus minimal care for knee and hip osteoarthritis, excluding high-risk-of-bias studies.

APPENDIX C

Weight

Study/Subgroup	SMD ± SE	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]			
Telephone coaching plus referral	−0.0564 ± 0.1155	14.1%	−0.06 (−0.28, 0.17)
Allen et al[2]			
Telephone coaching plus referral	−0.1526 ± 0.1421	13.8%	−0.15 (−0.43, 0.13)
Ghroubi et al[23]			
Reduced-calorie diet plus exercise	−0.5325 ± 0.51	8.7%	−0.53 (−1.53, 0.47)
Reduced-calorie diet	−0.1941 ± 0.5336	8.4%	−0.19 (−1.24, 0.85)
Miller et al[37]			
MR, reduced-calorie diet plus exercise	−1.7559 ± 0.2786	12.1%	−1.76 (−2.30, −1.21)
O'Brien et al[41]			
Telephone coaching	−0.015 ± 0.1833	13.4%	−0.01 (−0.37, 0.34)
Toda et al[56]			
Pharmacology plus MR	−2.7287 ± 0.4741	9.2%	−2.73 (−3.66, −1.80)
Wolf et al[60]			
Reduced-calorie diet plus exercise	−0.1344 ± 0.4018	10.3%	−0.13 (−0.92, 0.65)
Reduced-calorie diet	−0.6852 ± 0.4184	10.0%	−0.69 (−1.51, 0.13)
Total[a]		100.0%	−0.64 (−1.10, −0.18)

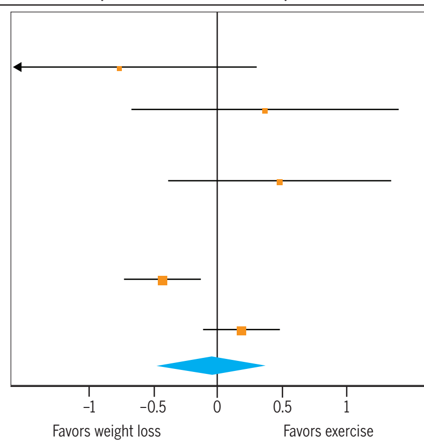


[a]*Heterogeneity: $\tau^2 = 0.38$, $\chi^2 = 62.72$, df = 8 (P<.0001), $I^2 = 87\%$. Test for overall effect: z = 2.70 (P = .007).*
Abbreviations: IV, inverse variance; MR, meal replacement; SE, standard error; SMD, standardized mean difference.

FIGURE 1 (CONTINUED). Weight-loss interventions versus minimal care for knee and hip osteoarthritis, excluding high-risk-of-bias studies.

Pain

Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	3.62 ± 1.9	12	5.28 ± 2.4	5	11.4%	−0.77 (−1.85, 0.31)
Reduced-calorie diet	6.08 ± 1.83	12	5.28 ± 2.4	5	11.9%	0.38 (−0.67, 1.43)
Messier et al[35]						
Reduced-calorie diet plus exercise	2.21 ± 1.247	12	1.57 ± 1.23	9	14.9%	0.50 (−0.38, 1.38)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	3.3 ± 2.436	129	4.35 ± 2.436	64	31.0%	−0.43 (−0.73, −0.13)
MR, reduced-calorie diet	4.8 ± 2.813	124	4.3 ± 1.985	63	30.9%	0.19 (−0.11, 0.50)
Total[a]		289		146	100.0%	−0.04 (−0.48, 0.40)



[a]*Heterogeneity: $\tau^2 = 0.14$, $\chi^2 = 12.16$, df = 4 (P = .02), $I^2 = 67\%$. Test for overall effect: z = 0.19 (P = .85).*
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

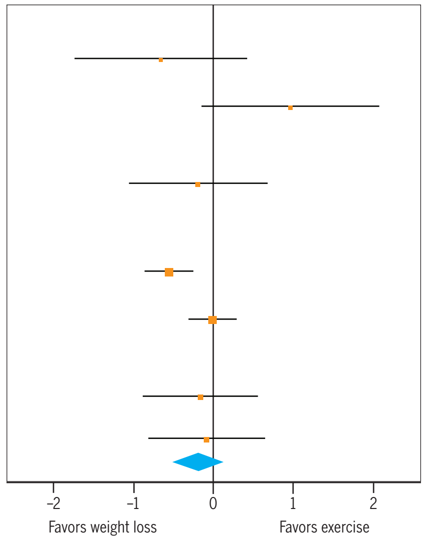
Figure continues on page B11.

FIGURE 2. Weight-loss interventions versus exercise-only interventions for knee osteoarthritis, excluding high-risk-of-bias studies.

APPENDIX C

Disability

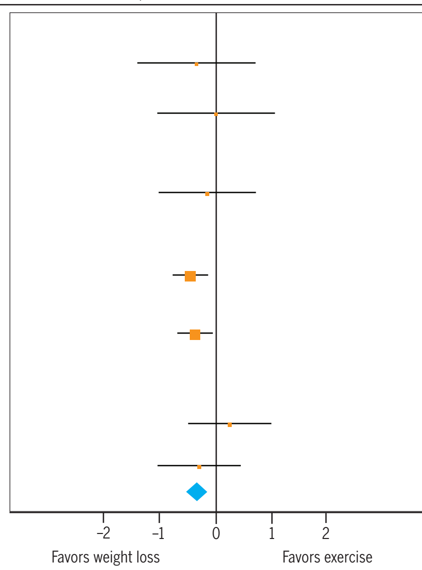
Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	6.08 ± 1.5	12	7.0 ± 0.72	5	6.9%	−0.65 (−1.73, 0.42)
Reduced-calorie diet	7.75 ± 0.75	12	7.0 ± 0.72	5	6.5%	0.96 (−0.15, 2.07)
Messier et al[35]						
Reduced-calorie diet plus exercise	1.42 ± 0.312	12	1.48 ± 0.3	9	9.5%	−0.19 (−1.05, 0.68)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	13.0 ± 7.608	129	17.21 ± 7.608	64	26.3%	−0.55 (−0.86, −0.25)
MR, reduced-calorie diet	17.3 ± 7.255	124	17.34 ± 7.255	63	26.3%	−0.01 (−0.31, 0.30)
Wolf et al[60]						
Reduced-calorie diet plus exercise	33.6 ± 11.4	20	35.4 ± 10.6	12	12.4%	−0.16 (−0.87, 0.56)
Reduced-calorie diet	34.4 ± 12	21	35.4 ± 10.6	11	12.1%	−0.08 (−0.81, 0.65)
Total[a]		330		169	100.0%	−0.18 (−0.49, 0.14)



[a]*Heterogeneity:* $\tau^2 = 0.07$, $\chi^2 = 11.61$, $df = 6$ ($P = .07$), $I^2 = 48\%$. *Test for overall effect:* $z = 1.10$ ($P = .27$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

Weight

Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	−6.21 ± 11.3	12	−2.38 ± 10.2	5	3.4%	−0.33 (−1.38, 0.72)
Reduced-calorie diet	−2.15 ± 11.7	12	−2.38 ± 10.2	5	3.4%	0.02 (−1.02, 1.06)
Messier et al[35]						
Reduced-calorie diet plus exercise	−18.8 ± 96.995	12	−4.0 ± 111.0	9	5.0%	−0.14 (−1.00, 0.73)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	−10.6 ± 19.445	121	−1.8 ± 21.112	58	37.4%	−0.44 (−0.75, −0.12)
MR, reduced-calorie diet	−8.9 ± 19.363	120	−1.8 ± 21.112	57	37.1%	−0.35 (−0.67, −0.04)
Wolf et al[60]						
Reduced-calorie diet plus exercise	−2.1 ± 5.6	20	−4.8 ± 15.3	11	6.9%	0.26 (−0.48, 1.00)
Reduced-calorie diet	−8.2 ± 10.1	24	−4.8 ± 15.3	10	6.8%	−0.28 (−1.02, 0.46)
Total[a]		321		155	100.0%	−0.31 (−0.51, −0.12)



[a]*Heterogeneity:* $\tau^2 = 0.00$, $\chi^2 = 3.54$, $df = 6$ ($P = .74$), $I^2 = 0\%$. *Test for overall effect:* $z = 3.18$ ($P = .001$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

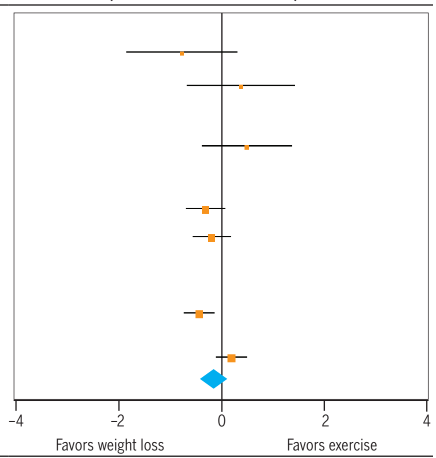
FIGURE 2 (CONTINUED). Weight-loss interventions versus exercise-only interventions for knee osteoarthritis, excluding high-risk-of-bias studies.

APPENDIX D

META-ANALYSIS RESULTS FOR PRIMARY OUTCOMES AND WEIGHT FOR 3 COMPARISONS

Pain

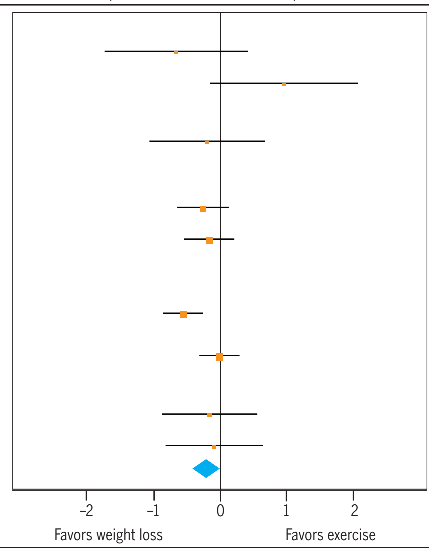
Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	3.62 ± 1.9	12	5.28 ± 2.4	5	5.2%	−0.77 (−1.85, 0.31)
Reduced-calorie diet	6.08 ± 1.83	12	5.28 ± 2.4	5	5.4%	0.38 (−0.67, 1.43)
Messier et al[35]						
Reduced-calorie diet plus exercise	2.21 ± 1.247	12	1.57 ± 1.23	9	7.2%	0.50 (−0.38, 1.38)
Messier et al[34]						
Reduced-calorie diet plus exercise	5.07 ± 4.097	76	6.24 ± 2.972	40	18.9%	−0.31 (−0.69, 0.08)
Reduced-calorie diet	5.51 ± 4.075	82	6.24 ± 2.972	40	19.1%	−0.19 (−0.57, 0.19)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	3.3 ± 2.436	129	4.35 ± 2.436	64	22.1%	−0.43 (−0.73, −0.13)
MR, reduced-calorie diet	4.8 ± 2.813	124	4.3 ± 1.985	63	22.0%	0.19 (−0.11, 0.50)
Total[a]		447		226	100.0%	−0.13 (−0.40, 0.14)



[a]*Heterogeneity:* $\tau^2 = 0.06$, $\chi^2 = 13.20$, $df = 6$ ($P = .04$), $I^2 = 55\%$. *Test for overall effect:* $z = 0.95$ ($P = .34$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

Disability

Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	6.08 ± 1.5	12	7.0 ± 0.72	5	3.4%	−0.65 (−1.73, 0.42)
Reduced-calorie diet	7.75 ± 0.75	12	7.0 ± 0.72	5	3.2%	0.96 (−0.15, 2.07)
Messier et al[35]						
Reduced-calorie diet plus exercise	1.42 ± 0.312	12	1.48 ± 0.3	9	4.9%	−0.19 (−1.05, 0.68)
Messier et al[34]						
Reduced-calorie diet plus exercise	17.87 ± 12.205	76	20.93 ± 11.628	40	16.5%	−0.25 (−0.64, 0.13)
Reduced-calorie diet	19.07 ± 11.772	82	20.93 ± 11.628	40	16.8%	−0.16 (−0.54, 0.22)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	13.0 ± 7.608	129	17.21 ± 7.608	64	20.9%	−0.55 (−0.86, −0.25)
MR, reduced-calorie diet	17.3 ± 7.255	124	17.34 ± 7.255	63	21.0%	−0.01 (−0.31, 0.30)
Wolf et al[60]						
Reduced-calorie diet plus exercise	33.6 ± 11.4	20	35.4 ± 10.6	12	6.8%	−0.16 (−0.87, 0.56)
Reduced-calorie diet	34.4 ± 12	21	35.4 ± 10.6	11	6.6%	−0.08 (−0.81, 0.65)
Total[a]		488		249	100.0%	−0.20 (−0.41, 0.00)



[a]*Heterogeneity:* $\tau^2 = 0.03$, $\chi^2 = 11.75$, $df = 8$ ($P = .16$), $I^2 = 32\%$. *Test for overall effect:* $z = 1.92$ ($P = .05$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

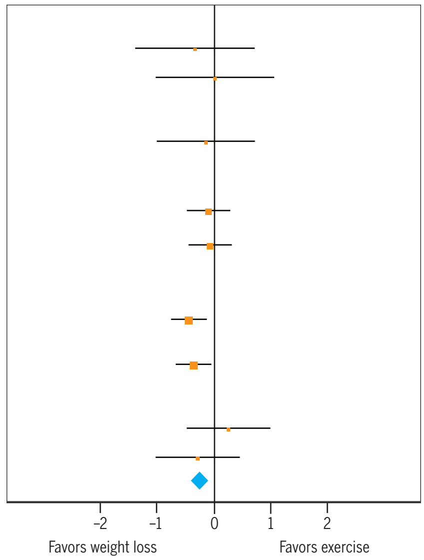
Figure continues on page B13.

FIGURE 1. Weight-loss interventions versus exercise-only interventions for knee osteoarthritis.

APPENDIX D

Weight

Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	−6.21 ± 11.3	12	−2.38 ± 10.2	5	2.2%	−0.33 (−1.38, 0.72)
Reduced-calorie diet	−2.15 ± 11.7	12	−2.38 ± 10.2	5	2.3%	0.02 (−1.02, 1.06)
Messier et al[35]						
Reduced-calorie diet plus exercise	−18.8 ± 96.995	12	−4.0 ± 111.0	9	3.3%	−0.14 (−1.00, 0.73)
Messier et al[34]						
Reduced-calorie diet plus exercise	−5.2 ± 19.036	76	−3.46 ± 19.008	40	16.8%	−0.09 (−0.47, 0.29)
Reduced-calorie diet	−4.61 ± 19.251	82	−3.46 ± 19.008	40	17.3%	−0.06 (−0.44, 0.32)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	−10.6 ± 19.445	121	−1.8 ± 21.112	58	24.6%	−0.44 (−0.75, −0.12)
MR, reduced-calorie diet	−8.9 ± 19.363	120	−1.8 ± 21.112	57	24.5%	−0.35 (−0.67, −0.04)
Wolf et al[60]						
Reduced-calorie diet plus exercise	−2.1 ± 5.6	20	−4.8 ± 15.3	11	4.5%	0.26 (−0.48, 1.00)
Reduced-calorie diet	−8.2 ± 10.1	24	−4.8 ± 15.3	10	4.5%	−0.28 (−1.02, 0.46)
Total[a]		479		235	100.0%	−0.23 (−0.39, −0.08)

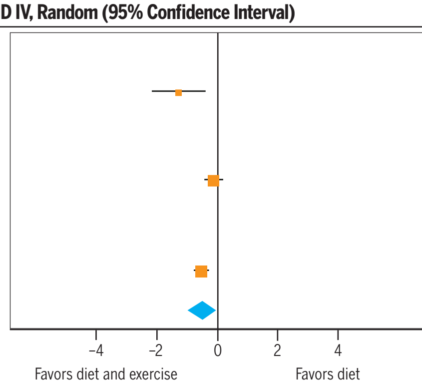


[a]Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 5.55$, df = 8 (P = .70), $I^2 = 0\%$. Test for overall effect: z = 2.90 (P = .004).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

FIGURE 1 (CONTINUED). Weight-loss interventions versus exercise-only interventions for knee osteoarthritis.

Pain

Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Diet Only Mean ± SD	Diet Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	3.62 ± 1.9	12	6.08 ± 1.83	12	17.0%	−1.27 (−2.17, −0.38)
Messier et al[34]						
Reduced-calorie diet plus exercise	5.07 ± 4.097	76	5.51 ± 4.075	82	40.1%	−0.11 (−0.42, 0.21)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	3.3 ± 2.840	129	4.78 ± 2.834	124	43.0%	−0.52 (−0.77, −0.27)
Total[a]		217		218	100.0%	−0.48 (−0.94, −0.03)



[a]Heterogeneity: $\tau^2 = 0.11$, $\chi^2 = 7.93$, df = 2 (P = .02), $I^2 = 75\%$. Test for overall effect: z = 2.09 (P = .04).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

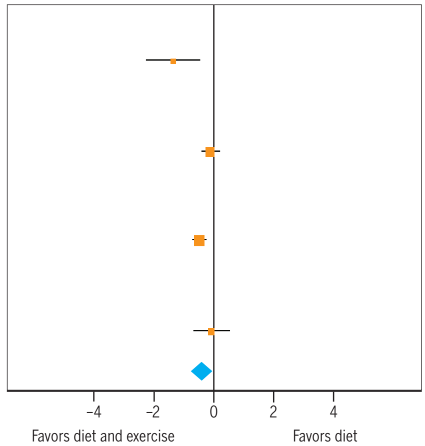
Figure continues on page B14.

FIGURE 2. Dietary weight-loss and exercise interventions versus dietary weight loss–only interventions for knee osteoarthritis.

APPENDIX D

Disability

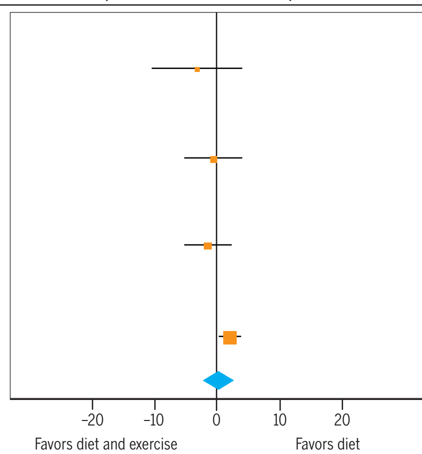
Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Diet Only Mean ± SD	Diet Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	6.08 ± 1.5	12	7.75 ± 0.75	12	12.3%	−1.36 (−2.26, −0.46)
Messier et al[34]						
Reduced-calorie diet plus exercise	17.87 ± 12.205	76	19.07 ± 11.772	82	32.5%	−0.10 (−0.41, 0.21)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	13.0 ± 8.925	129	17.25 ± 8.925	124	35.4%	−0.47 (−0.72, −0.22)
Wolf et al[60]						
Reduced-calorie diet plus exercise	33.6 ± 11.4	20	34.4 ± 12	21	19.9%	−0.07 (−0.68, 0.55)
Total[a]		237		239	100.0%	−0.38 (−0.76, 0.00)



[a]*Heterogeneity: τ^2 = 0.09, χ^2 = 9.04, df = 3 (P = .03), I^2 = 67%. Test for overall effect: z = 1.98 (P = .05).*
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

Weight

Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Diet Only Mean ± SD	Diet Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	−6.21 ± 11.3	12	−2.15 ± 11.7	12	9.2%	−4.06 (−13.26, 5.14)
Messier et al[34]						
Reduced-calorie diet plus exercise	−5.2 ± 19.036	76	−4.61 ± 19.251	82	18.3%	−0.59 (−6.56, 5.38)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	−10.6 ± 19.445	121	−8.9 ± 19.363	120	23.9%	−1.70 (−6.60, 3.20)
Wolf et al[60]						
Reduced-calorie diet plus exercise	−0.95 ± 2.5	20	−3.72 ± 4.6	24	48.7%	2.77 (0.63, 4.91)
Total[a]		229		238	100.0%	0.46 (−2.55, 3.48)



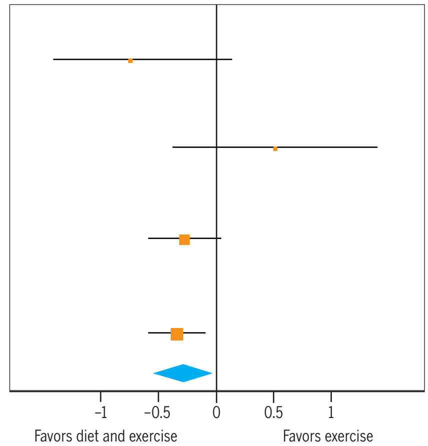
[a]*Heterogeneity: τ^2 = 3.66, χ^2 = 4.86, df = 3 (P = .18), I^2 = 38%. Test for overall effect: z = 0.30 (P = .76).*
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

FIGURE 2 (CONTINUED). Dietary weight-loss and exercise interventions versus dietary weight loss–only interventions for knee osteoarthritis.

APPENDIX D

Pain

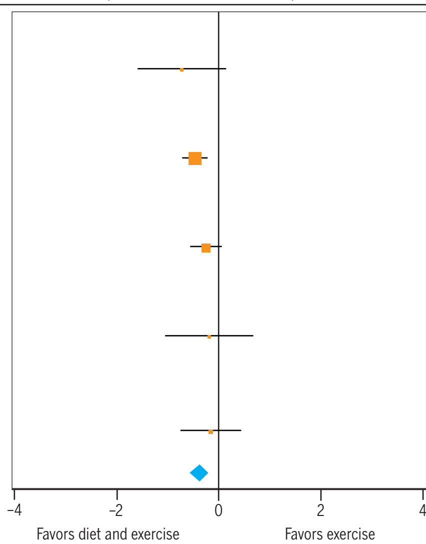
Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Exercise Only Mean ± SD	Exercise Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	3.62 ± 1.9	12	5.28 ± 2.4	10	7.9%	−0.75 (−1.62, 0.13)
Messier et al[35]						
Reduced-calorie diet plus exercise	2.21 ± 1.247	12	1.57 ± 1.23	9	7.8%	0.50 (−0.38, 1.38)
Messier et al[34]						
Reduced-calorie diet plus exercise	5.07 ± 4.097	76	6.24 ± 4.204	80	37.1%	−0.28 (−0.60, 0.04)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	3.3 ± 2.870	129	4.3 ± 2.847	127	47.2%	−0.35 (−0.60, −0.10)
Total[a]		229		226	100.0%	−0.29 (−0.55, −0.03)



[a]*Heterogeneity:* $\tau^2 = 0.02$, $\chi^2 = 4.30$, $df = 3$ ($P = .23$), $I^2 = 30\%$. *Test for overall effect:* $z = 2.19$ ($P = .03$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

Disability

Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Exercise Only Mean ± SD	Exercise Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	6.08 ± 1.5	12	7.0 ± 0.72	10	4.1%	−0.73 (−1.60, 0.14)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	13.0 ± 8.61	129	17.2 ± 9.111	127	51.1%	−0.47 (−0.72, −0.22)
Messier et al[34]						
Reduced-calorie diet plus exercise	17.87 ± 12.205	76	20.93 ± 11.628	80	31.8%	−0.26 (−0.57, 0.06)
Messier et al[35]						
Reduced-calorie diet plus exercise	1.42 ± 0.312	12	1.48 ± 0.3	9	4.2%	−0.19 (−1.05, 0.68)
Wolf et al[60]						
Reduced-calorie diet plus exercise	33.6 ± 11.4	20	35.4 ± 10.6	23	8.8%	−0.16 (−0.76, 0.44)
Total[a]		249		249	100.0%	−0.38 (−0.55, −0.20)



[a]*Heterogeneity:* $\tau^2 = 0.00$, $\chi^2 = 2.45$, $df = 4$ ($P = .65$), $I^2 = 0\%$. *Test for overall effect:* $z = 4.14$ ($P < .0001$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

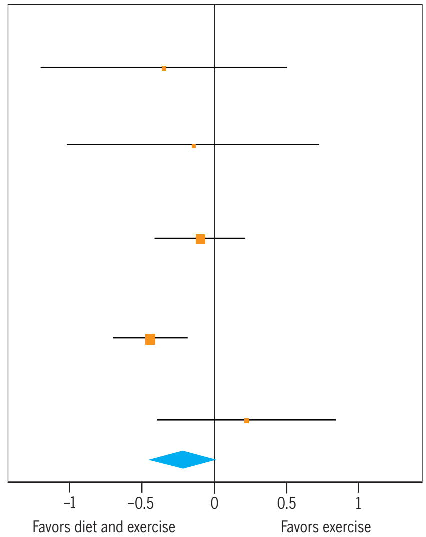
Figure continues on page B16.

FIGURE 3. Dietary weight-loss and exercise interventions versus exercise-only interventions for knee osteoarthritis.

APPENDIX D

Weight

Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Exercise Only Mean ± SD	Exercise Only Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	−6.21 ± 11.3	12	−2.38 ± 10.2	10	7.0%	−0.34 (−1.19, 0.51)
Messier et al[35]						
Reduced-calorie diet plus exercise	−18.8 ± 96.995	12	−4.0 ± 11.1	9	6.8%	−0.14 (−1.00, 0.73)
Messier et al[34]						
Reduced-calorie diet plus exercise	−5.2 ± 19.036	76	−3.46 ± 19.008	80	33.0%	−0.09 (−0.41, 0.22)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	−10.6 ± 19.445	121	−1.8 ± 21.112	115	40.8%	−0.43 (−0.69, −0.17)
Wolf et al[60]						
Reduced-calorie diet plus exercise	−2.1 ± 5.6	20	−4.8 ± 15.3	21	12.4%	0.23 (−0.39, 0.84)
Total[a]		241		235	100.0%	−0.21 (−0.45, 0.02)



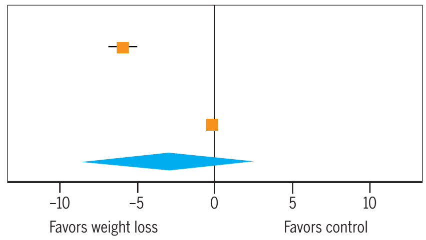
[a]*Heterogeneity:* $\tau^2 = 0.02$, $\chi^2 = 5.33$, $df = 4$ ($P = .26$), $I^2 = 25\%$. *Test for overall effect:* $z = 1.77$ ($P = .08$).
Abbreviations: IV, inverse variance; MR, meal replacement; SMD, standardized mean difference.

FIGURE 3 (CONTINUED). Dietary weight-loss and exercise interventions versus exercise-only interventions for knee osteoarthritis.

APPENDIX D

Pain

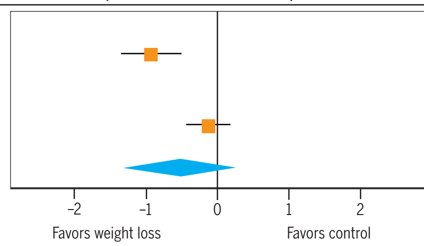
Study/Subgroup	Weight Loss		Usual Care		Weight	SMD IV, Random (95% Confidence Interval)
	Mean ± SD	Total, n	Mean ± SD	Total, n		
Muehlbacher et al[39]						
Pharmaceuticals	22.9 ± 1.4	48	34.3 ± 2.3	48	49.7%	−5.94 (−6.89, −4.99)
Williams et al[59]						
Telephone coaching and education	5.8 ± 2.7	79	6.3 ± 2.4	80	50.3%	−0.19 (−0.51, 0.12)
Total[a]		127		128	100.0%	-3.05 (−8.68, 2.58)



[a]*Heterogeneity: τ^2 = 16.37, χ^2 = 127.64, df = 1 (P<.0001), I^2 = 99%. Test for overall effect: z = 1.06 (P = .29).*
Abbreviations: IV, inverse variance; SMD, standardized mean difference.

Disability

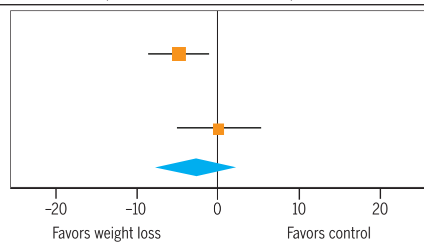
Study/Subgroup	Weight Loss		Usual Care		Weight	SMD IV, Random (95% Confidence Interval)
	Mean ± SD	Total, n	Mean ± SD	Total, n		
Muehlbacher et al[39]						
Pharmaceuticals	34.0 ± 5.2	48	38.9 ± 5.3	48	48.3%	−0.93 (−1.35, −0.50)
Williams et al[59]						
Telephone coaching and education	13.9 ± 6.5	79	14.7 ± 5.9	80	51.7%	−0.13 (−0.44, 0.18)
Total[a]		127		128	100.0%	−0.51 (−1.29, 0.27)



[a]*Heterogeneity: τ^2 = 0.28, χ^2 = 8.89, df = 1 (P = .003), I^2 = 89%. Test for overall effect: z = 1.29 (P = .20).*
Abbreviations: IV, inverse variance; SMD, standardized mean difference.

Weight

Study/Subgroup	Weight Loss		Usual Care		Weight	SMD IV, Random (95% Confidence Interval)
	Mean ± SD	Total, n	Mean ± SD	Total, n		
Muehlbacher et al[39]						
Pharmaceuticals	86.2 ± 9.5	48	91.0 ± 9.8	48	57.0%	−4.80 (−8.66, −0.94)
Williams et al[59]						
Telephone coaching and education	93.5 ± 17.4	79	93.3 ± 16.8	80	43.0%	0.20 (−5.12, 5.52)
Total[a]		127		128	100.0%	−2.65 (−7.50, 2.20)



[a]*Heterogeneity: τ^2 = 6.88, χ^2 = 2.22, df = 1 (P = .14), I^2 = 55%. Test for overall effect: z = 1.07 (P = .28).*
Abbreviations: IV, inverse variance; SMD, standardized mean difference.

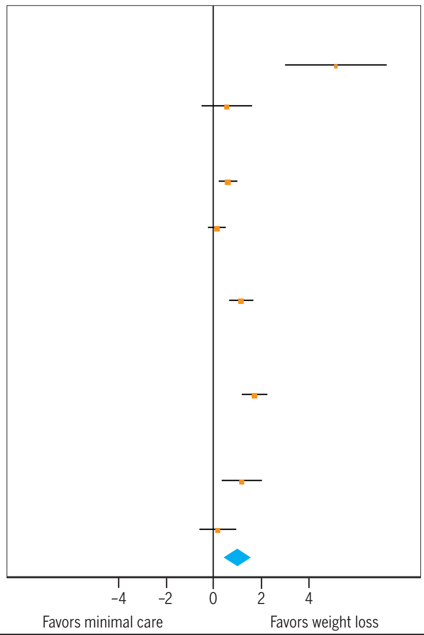
FIGURE 4. Weight-loss interventions versus controls for chronic low back pain.

APPENDIX E

META-ANALYSIS RESULTS FOR SECONDARY OUTCOMES (PHYSICAL PERFORM WEIGHT LOSS HEALTH, AND PHYSICAL ACTIVITY) FOR 4 COMPARISONS

Physical Performance

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Ghroubi et al[23]					
Reduced-calorie diet plus exercise	5.1301 ± 1.089	12	6	4.9%	5.13 (3.00, 7.26)
Reduced-calorie diet	0.5498 ± 0.5431	12	5	10.4%	0.55 (−0.51, 1.61)
Messier et al[34]					
Reduced-calorie diet plus exercise	0.5882 ± 0.2009	76	39	15.4%	0.59 (0.19, 0.98)
Reduced-calorie diet	0.1249 ± 0.1947	82	39	15.4%	0.12 (−0.26, 0.51)
Miller et al[37]					
MR, reduced-calorie diet plus exercise	1.1544 ± 0.2585	39	32	14.7%	1.15 (0.65, 1.66)
Saraboon et al[50]					
Reduced-calorie diet plus exercise plus education	1.7097 ± 0.2737	40	40	14.4%	1.71 (1.17, 2.25)
Wolf et al[60]					
Reduced-calorie diet plus exercise	1.1769 ± 0.4305	21	9	12.1%	1.18 (0.33, 2.02)
Reduced-calorie diet	0.1697 ± 0.3964	22	9	12.6%	0.17 (−0.61, 0.95)
Total[a]		304	179	100.0%	1.00 (0.44, 1.56)



[a]*Heterogeneity:* $\tau^2 = 0.50$, $\chi^2 = 45.14$, $df = 7$ ($P<.0001$), $I^2 = 84\%$. *Test for overall effect:* $z = 3.47$ ($P = .0005$).
Abbreviations: IV, inverse variance; MR, meal replacement; SE, standard error; SMD, standardized mean difference.

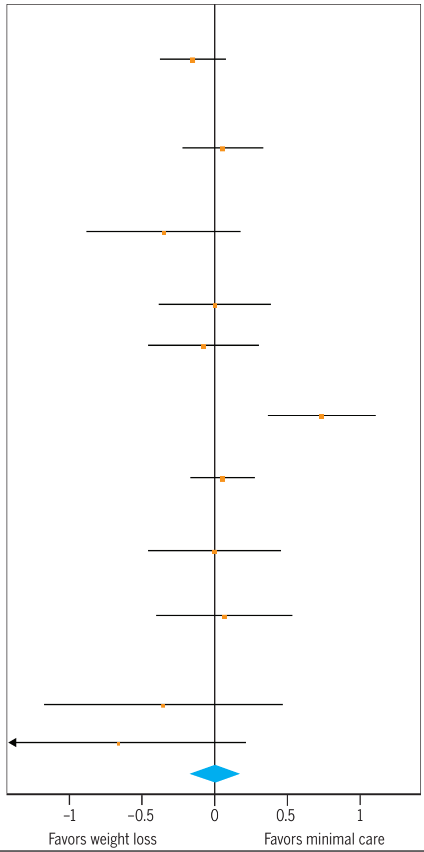
Figure continues on page B19.

FIGURE 1. Weight-loss interventions versus minimal care for knee and hip osteoarthritis.

APPENDIX E

Mental Health

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]					
Telephone coaching plus referral	−0.1505 ± 0.1156	151	149	14.2%	−0.15 (−0.38, 0.08)
Allen et al[2]					
Telephone coaching plus referral	0.0566 ± 0.1419	151	74	12.6%	0.06 (−0.22, 0.33)
Lim et al[33]					
Exercise only	−0.351 ± 0.2697	46	20	6.8%	−0.35 (−0.88, 0.18)
Messier et al[34]					
Reduced-calorie diet plus exercise	0.0009 ± 0.197	76	39	9.6%	0.00 (−0.39, 0.39)
Reduced-calorie diet	−0.0766 ± 0.1946	82	39	9.8%	−0.08 (−0.46, 0.30)
O'Brien et al[41]					
Telephone coaching	0.7357 ± 0.1897	59	60	10.0%	0.74 (0.36, 1.11)
Ravaud et al[43]					
Counseling plus education	0.054 ± 0.1127	146	171	14.4%	0.05 (−0.17, 0.27)
Somers et al[53]					
Reduced-calorie diet plus exercise plus PCS	0.0 ± 0.2336	62	26	8.0%	0.00 (−0.46, 0.46)
Reduced-calorie diet plus exercise	0.0661 ± 0.2387	59	25	7.8%	0.07 (−0.40, 0.53)
Wolf et al[60]					
Reduced-calorie diet plus exercise	−0.3532 ± 0.4185	21	8	3.5%	−0.35 (−1.17, 0.47)
Reduced-calorie diet	−0.66 ± 0.4467	21	7	3.2%	−0.66 (−1.54, 0.22)
Total[a]		874	618	100.0%	0.01 (−0.16, 0.18)



[a]*Heterogeneity: τ^2 = 0.04, χ^2 = 21.86, df = 10 (P = .02), I^2 = 54%. Test for overall effect: z = 0.09 (P = .93).*
Abbreviations: IV, inverse variance; PCS, pain coping skills; SE, standard error; SMD, standardized mean difference.

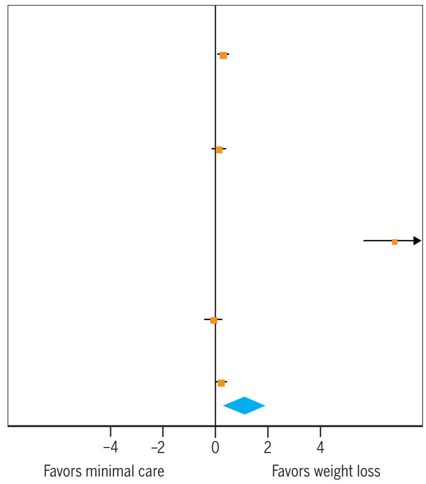
Figure continues on page B20.

FIGURE 1 (CONTINUED). Weight-loss interventions versus minimal care for knee and hip osteoarthritis.

APPENDIX E

Physical Activity

Study/Subgroup	SMD ± SE	Experimental Total, n	Control Total, n	Weight	SMD IV, Random (95% Confidence Interval)
Allen et al[3]					
Telephone coaching plus referral	0.298 ± 0.1161	151	149	21.6%	0.30 (0.07, 0.53)
Allen et al[2]					
Telephone coaching plus referral	0.1329 ± 0.142	151	74	21.4%	0.13 (−0.15, 0.41)
Miller et al[37]					
MR, reduced-calorie diet plus exercise	6.8348 ± 0.6055	39	39	14.4%	6.83 (5.65, 8.02)
O'Brien et al[41]					
Telephone coaching	−0.0647 ± 0.1834	59	60	21.0%	−0.06 (−0.42, 0.29)
Ravaud et al[43]					
Counseling plus education	0.2218 ± 0.1159	146	181	21.6%	0.22 (−0.01, 0.45)
Total[a]		546	503	100.0%	1.11 (0.34, 1.88)



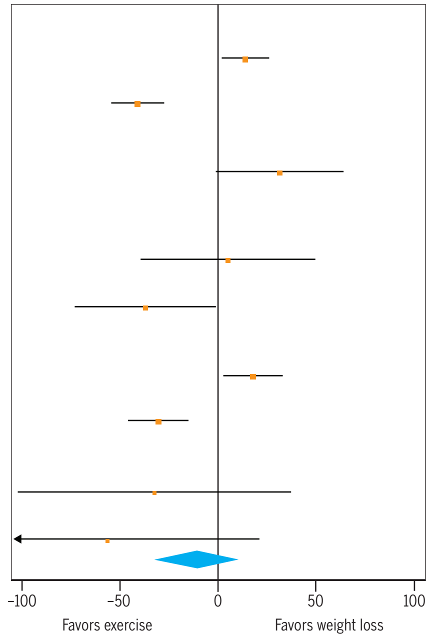
[a]*Heterogeneity: $\tau^2 = 0.70$, $\chi^2 = 122.04$, df = 4 ($P<.0001$), $I^2 = 97\%$. Test for overall effect: z = 2.84 ($P = .005$).*
Abbreviations: IV, inverse variance; MR, meal replacement; SE, standard error; SMD, standardized mean difference.

FIGURE 1 (CONTINUED). Weight-loss interventions versus minimal care for knee and hip osteoarthritis.

APPENDIX E

Physical Performance

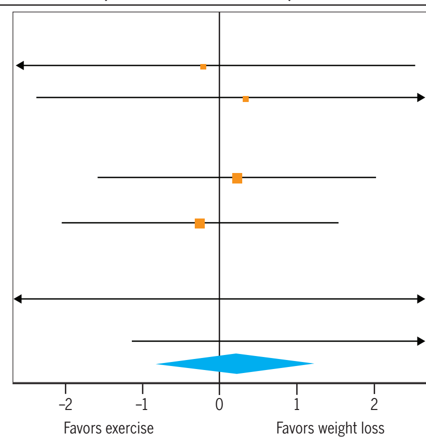
Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	MD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	480.0 ± 10.4	12	466.0 ± 12.13	5	14.6%	14.00 (1.85, 26.15)
Reduced-calorie diet	425.0 ± 14.8	12	466.0 ± 12.13	5	14.4%	−41.00 (−54.53, −27.47)
Messier et al[35]						
Reduced-calorie diet plus exercise	555.04 ± 38.001	12	523.64 ± 37.47	9	11.4%	31.40 (−1.18, 63.98)
Messier et al[34]						
Reduced-calorie diet plus exercise	477.76 ± 114.377	76	472.73 ± 117.349	40	9.3%	5.03 (−39.51, 49.57)
Reduced-calorie diet	435.63 ± 116.633	82	472.73 ± 117.349	80	10.8%	−37.10 (−73.14, −1.06)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	548.0 ± 46.776	116	530.2 ± 46.776	53	14.2%	17.80 (2.60, 33.00)
MR, reduced-calorie diet	499.0 ± 46.778	107	529.5 ± 46.778	53	14.2%	−30.50 (−45.90, −15.10)
Wolf et al[60]						
Reduced-calorie diet plus exercise	486.54 ± 92.6	21	518.98 ± 101.4	12	5.9%	−32.44 (−102.15, 37.27)
Reduced-calorie diet	462.52 ± 125.4	22	518.98 ± 101.4	12	5.2%	−56.46 (−134.16, 21.24)
Total[a]		460		269	100.0%	−10.47 (−32.20, 11.26)



[a]Heterogeneity: $\tau^2 = 804.24$, $\chi^2 = 65.11$, $df = 8$ ($P<.0001$), $I^2 = 88\%$. Test for overall effect: $z = 0.94$ ($P = .34$).
Abbreviations: IV, inverse variance; MD, mean difference; MR, meal replacement.

Mental Health

Study/Subgroup	Experimental Mean ± SD	Experimental Total, n	Control Mean ± SD	Control Total, n	Weight	MD IV, Random (95% Confidence Interval)
Messier et al[34]						
Reduced-calorie diet plus exercise	53.84 ± 7.149	76	54.06 ± 7.245	40	14.4%	−0.22 (−2.98, 2.54)
Reduced-calorie diet	54.39 ± 7.063	82	54.06 ± 7.245	40	14.8%	0.33 (−2.39, 3.05)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	56.0 ± 5.905	124	55.78 ± 5.905	61	33.4%	0.22 (−1.59, 2.03)
MR, reduced-calorie diet	55.5 ± 5.840	124	55.76 ± 5.840	60	33.8%	−0.26 (−2.06, 1.54)
Wolf et al[60]						
Reduced-calorie diet plus exercise	52.38 ± 10.6	21	47.97 ± 11.4	12	1.8%	4.41 (−3.47, 12.29)
Reduced-calorie diet	54.52 ± 9.8	21	47.97 ± 11.4	12	1.8%	6.55 (−1.14, 14.24)
Total[a]		448		225	100.0%	0.20 (−0.84, 1.25)



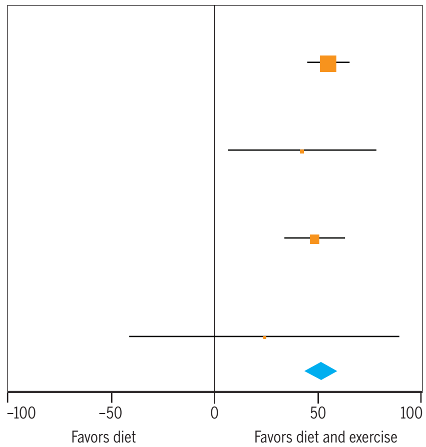
[a]Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 4.06$, $df = 5$ ($P = .54$), $I^2 = 0\%$. Test for overall effect: $z = 0.38$ ($P = .71$).
Abbreviations: IV, inverse variance; MD, mean difference; MR, meal replacement.

FIGURE 2. Weight-loss interventions versus exercise-only interventions for knee osteoarthritis.

APPENDIX E

Physical Performance

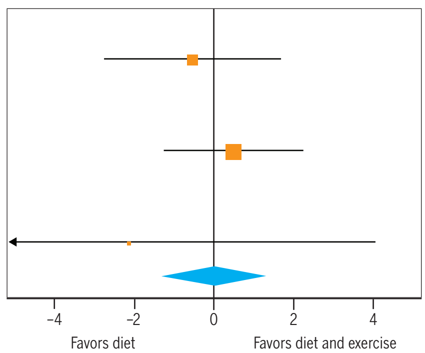
Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Diet Only Mean ± SD	Diet Only Total, n	Weight	MD IV, Random (95% Confidence Interval)
Ghroubi et al[23]						
Reduced-calorie diet plus exercise	480.0 ± 10.4	12	425.0 ± 14.8	12	62.9%	55.00 (44.77, 65.23)
Messier et al[34]						
Reduced-calorie diet plus exercise	477.76 ± 114.378	76	435.63 ± 116.633	82	5.1%	42.13 (6.09, 78.17)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	548.0 ± 55.955	116	499.7 ± 55.955	107	30.5%	48.30 (33.60, 63.00)
Wolf et al[60]						
Reduced-calorie diet plus exercise	486.54 ± 92.6	21	462.52 ± 125.4	22	1.5%	24.02 (–41.66, 89.70)
Total[a]		225		223	100.0%	51.83 (43.71, 59.95)



[a]*Heterogeneity:* $\tau^2 = 0.00$, $\chi^2 = 1.56$, $df = 3$ ($P = .67$), $I^2 = 0\%$. *Test for overall effect:* $z = 12.51$ ($P<.0001$).
Abbreviations: IV, inverse variance; MD, mean difference; MR, meal replacement.

Mental Health

Study/Subgroup	Diet and Exercise Mean ± SD	Diet and Exercise Total, n	Diet Only Mean ± SD	Diet Only Total, n	Weight	MD IV, Random (95% Confidence Interval)
Messier et al[34]						
Reduced-calorie diet plus exercise	53.84 ± 7.149	76	54.39 ± 7.063	82	36.6%	–0.55 (–2.77, 1.67)
Messier et al[36]						
MR, reduced-calorie diet plus exercise	56.0 ± 7.031	124	55.52 ± 7.031	124	58.7%	0.48 (–1.27, 2.23)
Wolf et al[60]						
Reduced-calorie diet plus exercise	52.38 ± 10.6	21	54.52 ± 9.8	21	4.7%	–2.14 (–8.31, 4.03)
Total[a]		221		227	100.0%	–0.02 (–1.36, 1.32)



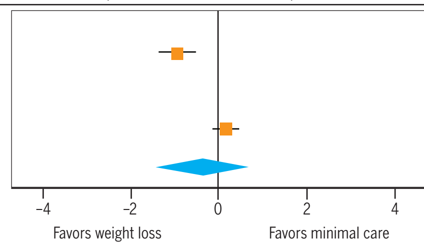
[a]*Heterogeneity:* $\tau^2 = 0.00$, $\chi^2 = 0.99$, $df = 2$ ($P = .61$), $I^2 = 0\%$. *Test for overall effect:* $z = 0.03$ ($P = .98$).
Abbreviations: IV, inverse variance; MD, mean difference; MR, meal replacement.

FIGURE 3. Dietary weight-loss interventions and exercise versus dietary weight loss only for knee osteoarthritis.

APPENDIX E

Mental Health

	Diet and Exercise		Usual Care			
Study/Subgroup	**Mean ± SD**	**Total, n**	**Mean ± SD**	**Total, n**	**Weight**	**SMD IV, Random (95% Confidence Interval)**
Muehlbacher et al[39]						
Pharmaceuticals	−72.9 ± 5.5	48	−67.5 ± 5.8	48	49.1%	−0.95 (−1.37, −0.52)
Williams et al[59]						
Telephone coaching and education	46.5 ± 13.8	79	44.3 ± 13.3	80	50.9%	0.16 (−0.15, 0.47)
Total[a]		127		128	100.0%	−0.38 (−1.47, 0.70)



[a]*Heterogeneity:* $\tau^2 = 0.58$, $\chi^2 = 17.14$, *df* = 1 (*P*<.0001), $I^2 = 94\%$. *Test for overall effect:* $z = 0.69$ (*P* = .49).
Abbreviations: IV, inverse variance; SMD, standardized mean difference.

FIGURE 4. Weight-loss interventions versus minimal care for chronic low back pain.