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Alternative models to support weight loss in chronic musculoskeletal conditions: Effectiveness of a physiotherapist-delivered intensive diet program for knee osteoarthritis, the POWER randomized controlled trial.

Kim Allison[1*], Sarah E Jones[1], Rana S Hinman[1], Jesse Pardo[1], Peixuan Li[2,3], Anurika P De Silva[2,3], Jonathan G Quicke[4,5], Priya Sumithran[6,7], Jodie Prendergast[8], Elena S George[9], Melanie A Holden[4], Nadine E Foster[4,10], Kim L Bennell[1]

[1]Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, The University of Melbourne, Melbourne, Australia Level 7 Barry Street Parkville,

[2]Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Australia

[3]Methods and Implementation Support for Clinical and Health research Hub, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Australia

[4]School of Medicine, Keele University, Keele, United Kingdom

[5]Chartered Society of Physiotherapy, Chancery Exchange, London, United Kingdom.

[6]Department of Surgery, Central Clinical School, Monash University, Australia

[7] Department of Endocrinology and Diabetes, Alfred Health, Melbourne, Australia

[8] Medibank Private, Melbourne, Australia

[9] Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Deakin University, Melbourne, Australia

[10] STARS Education and Research Alliance, Surgical Treatment and Rehabilitation Service (STARS), The University of Queensland and Metro North Health, Brisbane, Australia

*** Corresponding author:** Kim Allison[1], Centre for Health, Exercise & Sports Medicine, University of Melbourne, kim.allison@unimelb.edu.au, Ph:03 90354860

Abstract

Objective: To determine if physiotherapists can deliver a clinically effective very low energy diet (VLED) supplementary to exercise in people with knee osteoarthritis (OA) and overweight or obesity.

Methods: 88 participants with knee OA and body mass index (BMI) >27 kg/m^2 were randomized to either Intervention (n=42: VLED including two daily meal replacement products supplementary to Control) or Control (n=46: exercise), Both interventions were delivered by unblinded physiotherapists via six videoconference sessions over six months. Primary outcome was percentage change in body weight at six months measured by a blinded assessor. Secondary outcomes included BMI, waist circumference, waist-to-hip-ratio, self-reported measures of pain, function, satisfaction and perceived global change, and physical performance tests.

Results: The Intervention group lost a mean (standard deviation) 8.1 (5.2)% body weight compared with 1.0 (3.2)% Control (mean (95% confidence interval) between-group difference 7.2 (5.1, 9.3)%, p<0.001), with significantly lower BMI and waist circumference compared to Control at follow up. 75% of participants in the Intervention group achieved ≥5% body weight loss, 37% ≥10% compared with 12% and 0% respectively in Control. More participants in Intervention [27/38 (71.1%)] reported global knee improvement than in Control [20/42 (47.6%)] (p=0.02). There were no between-group differences in any other secondary outcomes. No serious adverse events were reported.

Conclusion: A VLED delivered by physiotherapists achieved clinically relevant weight loss, and was safe, in people with knee OA and overweight or obesity. Results have potential implications for future service models of care for OA and obesity.

Trial registration: NIH US National Library of Medicine, Clinicaltrials.gov NCT04733053 (Feb 1, 2021)

Key words

Osteoarthritis, OA, Knee, Telehealth, Overweight, Obesity, Weight management, Physiotherapy, Very low energy diet, Exercise, Physical activity, Clinical trial, RCT

Summary box

What is already known on this topic

- A dietitian-delivered very low energy diet, alongside physiotherapist-delivered exercise, is effective for weight loss and symptoms in people with knee OA, however, access to dietitians for management of musculoskeletal conditions is limited for many people.
- While physiotherapists are also well placed to deliver weight loss support for synergistic benefit to exercise in people with knee OA, no studies have evaluated the effectiveness and safety of a physiotherapist-delivered weight loss intervention.

What this study adds

- This is the first study to show that physiotherapists can deliver a very low energy diet program, in addition to exercise, that was effective for weight loss and safe in people with knee OA.
- The diet and exercise group lost 8.1% body weight over six months, comparable to that achieved with dietitians in previous studies, with over a third of participants losing over 10% body weight.

How this study might affect research, practice, or policy

- This study provides the first proof-of-concept evidence of an alternate allied health clinician delivery model for weight loss in people with knee OA, which may guide future research and policy in the face of rising obesity rates and challenges facing healthcare systems

Background

Knee osteoarthritis (OA) is a major cause of pain and disability globally, affecting over 350 million adults [1]. Overweight and obesity are significant risk factors for knee OA progression [2], and rising rates of both obesity [3] and OA [1] are placing unprecedented demands on healthcare systems worldwide. International clinical guidelines for the management of knee OA include weight management as a core treatment where appropriate,[4] alongside exercise. However, for many people with OA and overweight or obesity, weight management support or referral for support is not routinely provided [5 6] or accessible due to workforce challenges. Innovative care models that expand practice roles of healthcare practitioners may increase patient access to weight management support.

As providers of lifestyle and exercise management for people with knee OA, there is an opportunity for physiotherapists to engage in extended scope weight loss support alongside exercise prescription to optimize management [7-12]. Nonetheless, upskilling is required as many physiotherapists currently lack confidence and the requisite competencies in weight management [12 13]. We have shown that a customized self-directed e-learning program for physiotherapists can increase physiotherapists' confidence in both knowledge and skills in lifestyle-interventions for weight management for patients with knee OA [14]. However, no studies have investigated the efficacy and safety of a physiotherapist-delivered weight loss program in any patient population.

Clinical guidelines for OA do not specify a dietary approach for weight loss [4] but meta-analysis data indicate that people adhering to a very low energy diet (VLED) over a 12-week period

frequently achieve the desired target of five percent body weight loss [15] thought to be required for symptomatic benefits [16 17]. Importantly, we have shown a VLED delivered by dietitians was effective [18] and acceptable to people with knee OA [19]. The nutritionally complete composition of a VLED diet using meal replacements means that healthcare practitioners without formal nutrition qualifications, such as physiotherapists, may be capable of effectively and safely supporting a VLED for selected people with knee OA.

We aimed to evaluate whether physiotherapists could effectively deliver a 6-month telehealth intensive dietary weight loss program, in addition to exercise a core recommended treatment for knee OA. [4] Our primary hypothesis was that a diet program combined with exercise (Intervention) would lead to greater weight loss than exercise (Control) at 6 months.

Methods

This was a two-group, superiority, parallel-design randomized controlled trial (RCT) prospectively registered (Clinicaltrials.gov NCT04733053), protocol published [20], approved by the University of Melbourne Human Research Ethics Committee (HREC 1955042). The only change to trial methods was allowing participants to self-report follow-up body weight over the telephone using their own scales if unable to attend follow-up.

Patient and public involvement

During project development, people with knee OA and physiotherapists were interviewed to understand the acceptability of a physiotherapist-delivered weight loss program [11 12] and study resources developed with input from people with knee OA [21].

Participants

Participants were recruited via print/radio/social media advertisements and our volunteer database. Inclusion criteria were: diagnosis of knee OA using National Institute for Health and Care Excellence clinical OA criteria (age≥45 years; activity-related knee pain; no knee morning stiffness ≥30 minutes) [22]; history of knee pain ≥ 3 months; knee pain on most days of past month; knee pain during walking over past week of ≥4 on an 11-point numeric rating scale (NRS); body mass index (BMI) >27 kg/m^2; willing to monitor blood pressure if using hypertensive medication and light-headed/dizzy during the trial; able to give informed consent and participate fully in trial procedures. Exclusion criteria are included in Supplement 1.

Randomization and blinding

Two randomization lists were computer-generated by an independent biostatistician. Participants were randomly allocated, first to physiotherapist in a 1:1 ratio, using permuted blocks of sizes 6 and 12, and then to treatment group in a 1:1 ratio, using permuted blocks of sizes 2 and 4, stratified by physiotherapist and participant sex [23 24]. Allocation was concealed in password-protected software (REDCap™) [25] and revealed following baseline assessment by a researcher not involved in recruitment or assessment. A blinded assessor collected primary outcome and

physical performance measures at 6 months and was a different person from the one collecting baseline data to negate unblinding due to physically obvious weight loss. It was not possible to blind physiotherapists or participants.

Physiotherapists and training

We recruited six (2 female, 4 male) physiotherapists in private practice in Melbourne, Australia who completed ~20 hours of mandatory training including: (i) self-directed e-learning modules (~10-12 hours over 6 weeks, previously described and evaluated [14] and since launched for clinicians (www.futurelean.com/courses/eduweight)) and additional trial protocol specific modules; (ii) six practice consultations delivering sessions 1, 2 and 4 of the VLED program to one 'mock' patient (research team member) and one 'practice' patient with knee OA. Sessions were audio-recorded, and a researcher provided itemized and patient feedback. Physiotherapists participated in a final hour-long teleconference to clarify study procedures.

Treatment groups

Participants in both groups consulted their physiotherapist via videoconference using Zoom (Zoom Video Communications, Inc., USA) for six sessions over six months. Participants were provided with hard copy OA educational resources, activity booklets, logbooks, and resistance bands (Appendix 1). Physiotherapists used semi-structured electronic consultation notes containing scripts, prompts and checklists for each consultation to enhance protocol fidelity.

a) Control

Consultations lasted 30 minutes initially, 20 minutes thereafter. Physiotherapists prescribed a home exercise program (5-6 lower limb strengthening exercises performed three times per week, (Appendix Table 2) from an established program [18 26 27], exercising at a moderate intensity (≥5 out of 10 ('hard') on a modified Borg Rating of Perceived Exertion scale [28]). A personalized, progressive physical activity plan was collaboratively developed with the participant.

b) Intervention

Consultations lasted 75 minutes initially (45 minutes diet component), 50 minutes thereafter (30 minutes diet component). Exercise components were the same as for the Control. Participants received Optifast (Nestlé Health Science, Rhodes, Australia) or Optislim (Optipharm, Australia) meal replacements, at no cost to themselves, for the first 14 weeks and additional hardcopy dietary/behavioural resources [18] (Appendix 1).

The diet intervention included three physiotherapist-supported phases (Table 1). Phase 1 'Weight loss' (0 to ≤ 12 weeks): aim ≥10% body weight loss via a VLED (two meal replacement products per day). Phase 2 'Transition': (once 10% weight loss was achieved/week 13 whichever came first, unless participants wanted to continue self-funding meal replacement products), participants were supported to transition over two weeks to a longer-term eating plan (reducing meal replacements, re-incorporating low glycaemic index carbohydrates). Phase 3 'Weight maintenance': healthy diet in concordance with the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Total Wellbeing diet [29]. If participants regained 2 kg or more, they were advised to re-commence two meal replacements per day for 1–2 weeks.

184

185 **Outcome measures**

186

187 Change in body weight from baseline to six months, expressed as a percentage, was the primary
188 outcome ((baseline-follow up)/baseline x100%). Body weight was measured at baseline and 6
189 months on the same set of calibrated digital laboratory platform scales (TCS-2 series)
190 (participants in bare feet and light clothing).

191

192 Secondary outcomes, (baseline and six-months), included: BMI; Waist circumference at mid-
193 abdomen level at its smallest circumference; Waist-to-hip ratio (waist circumference divided by
194 hip circumference); Average knee pain on walking in the last week using an 11-point NRS ('no
195 pain'='0' and 'worst pain possible'='10' [30]; Intermittent (scored 0-24) and constant (scored 0-
196 20) osteoarthritis pain measure (iCOAP) [31] (higher scores indicating higher pain); Physical
197 function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index
198 (WOMAC) [32] (0-68, higher scores indicating greater dysfunction); Perceived global change in
199 knee problems (7-point Likert scale from 'much worse' to 'much better' [33]) at 6-months
200 ('moderately better' or 'much better' categorized as 'improved'); Assessment of Quality of Life
201 (AQoL) (version AQoL-6D) [34], (-0.04 to 1.0, higher scores indicating higher quality of life);
202 Physical activity scale for the elderly (PASE) [35] (0 to 400, higher scores indicating greater
203 physical activity levels); Weight Self-Stigma Questionnaire (WSSQ) [36] (0-60, higher scores
204 indicating greater internalized weight stigma); Physical performance measures [37] including 30
205 sec chair sit-to-stand test (n), 40m fast-paced walk test (m/s) and 6-step stair climb test (sec),
206 where greater number, faster speed and shorter time taken respectively indicate better physical

function; Maximum voluntary isometric knee extensor strength (Nm/kg) from three repetitions, measured on an isokinetic dynamometer (HUMAC, CSI, Boston), knee at 60 degrees flexion.

Adherence and fidelity measures

Adherence measures included: Number of consultations attended (0-6); Self-reported number of prescribed home exercise sessions in the last two weeks at 6 months; Self-rated adherence to the home strengthening program, physical activity plan, and diet program (Intervention only), (separate 11-point NRS, higher scores indicating greater adherence); Total number of weeks meal replacements used (Intervention only).

Physiotherapist fidelity to the protocol was assessed from electronic consultation notes and reported as: Consultation duration (minutes); and Proportion of participants where required elements of diet and exercise components were delivered.

Other measures

Participant satisfaction with their intervention was assessed using a 7-point global rating scale ('extremely dissatisfied', to 'extremely satisfied', 'moderately' or 'extremely' satisfied categorized as 'satisfied'). Other process measures collected and a nested qualitative study of participants and physiotherapists [20] will be reported separately.

Descriptive measures and expectation of treatment outcome (self-reported via 5-point Likert scale, 'no effect at all' to 'complete recovery') were collected at baseline. At 6 months,

participants reported co-interventions used to manage their knee pain and weight during the trial. Adverse events were reported in the 6-month questionnaire.

Trial sample size

The trial was powered to detect a between-group difference in weight loss of 5% of body weight assuming no weight loss in the Control group [38 39]. While the between-participant standard deviation of percentage change in body weight was 5% in another study [39], we assumed a conservative standard deviation of 7.5% given that our program had less clinician contact [39]. For a power of 0.8 and a two-tailed significance level of 0.05, we required 37 participants per group, increased to 44 allowing for 15% loss to follow up [18].

Data analysis

A priori statistical analysis plan was developed. Biostatisticians (PL,ADS) analysed data blinded to group name. Comparative analyses between groups used all randomized participants based on the intention-to-treat principle. Missing outcomes were multiply imputed, separately by group, using chained equations and predictive mean matching with five nearest neighbours. See Supplementary Material 2 for further details on handling missing data.

The primary outcome, percentage change in body weight was compared between groups using a linear regression modelling adjusted for baseline weight to obtain an estimated mean difference, corresponding two-sided 95% confidence interval and p-value. Similar analyses were conducted for continuous secondary outcomes. Binary secondary outcomes were compared between groups

using log-binomial regression, with adjustment for baseline weight for achieving different weight loss %. In the case of rare events, binary outcomes were analyzed using Firth logistic regression [40]. Estimated risk differences and risk ratios, corresponding two-sided 95% confidence intervals and p-values were obtained. A sensitivity analysis was performed for the primary outcome, excluding those participants who self-reported follow-up body weight. An exploratory subgroup analysis for the primary outcome was conducted for the subgroups of BMI ($\geq$ 30 kg/m^2 vs <30kg/m^2), by fitting a linear regression model, adjusted for baseline weight with an interaction term between treatment group and subgroup in the model. All models were adjusted for stratification variables of sex and physiotherapist. Standard diagnostic plots were used to check model assumptions. No adjustment for multiple testing were conducted. All statistical analyses were conducted using Stata 17.0 [41].

Equity, Diversity and Inclusion

Our authors comprise early, mid-career and senior researchers from different disciplines across multiple countries. A full description of participant characteristics is included in Table 1, Supplementary Table 1. Accessibility was prioritized, with care delivered via freely available software, meal replacements provided at no cost and protocol modification to allow self-reported weight at follow-up.

Results

Participant characteristics

88 participants (42 Intervention) were enrolled from 507 people screened between October 2021 and October 2022, follow up completed May 2023 (Figure 1). Baseline participant characteristics

and treatment expectations were comparable between groups (Table 2). The primary outcome was completed by 38/42 (91%) participants in the Intervention and 42/46 (91%) in Control groups (Supplementary Table 1), with one participant in the Intervention and three in Control self-reporting weight.

Primary outcome

Physiotherapists were able to effectively deliver a weight loss program as shown by a mean (standard deviation) percentage body weight loss in the Intervention group of 8.1 (5.2)% compared to 1.0 (3.2)% in the Control (between-group mean (95% confidence interval (CI)) difference, 7.2 (5.1, 9.3)%), (Table 3). A greater proportion of Intervention participants achieved at least 5% [29/38 (76.3%)] and 10% [14/38 (36.8%)] weight loss than in Control [5/42 (11.9%); 0/42 (0%), respectively] (Table 4). Analysis using complete case data (Supplementary Tables 2 & 3) and sensitivity analysis excluding 4 (4.5%) participants who provided self-reported body weight at follow up showed similar results (Supplementary Table 4). The percentage weight loss achieved by Intervention participants allocated to each physiotherapist was variable ranging from 5.3% to 10.2% (Supplementary Table 6). We observed negligible differences in the effect of the intervention on the primary outcome between BMI subgroups ($\geq$30kg/m^2, <30kg/m^2) (Supplementary Table 5).

Secondary outcomes

There was a greater reduction in BMI and waist circumference with Intervention than Control, but no between-group difference for changes in waist-to-hip ratio, pain, function, quality-of-life, physical activity, weight self-stigma or physical performance measures (Table 3). More

participants in Intervention [27/38 (71.1%)] reported global knee improvement than in Control [20/42 (47.6%)] (Table 4).

Treatment and protocol adherence and satisfaction

There was generally good adherence to diet and exercise components in both groups, with number of consultations attended and exercise sessions comparable between groups (Table 5). All participants in Intervention attempted the VLED, with meal replacements used for a mean (SD) of 16 (6.4) weeks. More participants in Intervention were satisfied with their program [36/38 (95%)] than in Control [26/42 (62%)] (Table 5).

Physiotherapist fidelity to the protocol in both groups was excellent (Supplementary Table 8). A strengthening program was prescribed for all, and a physical activity plan for 83/88 (94%) participants in both groups. The mean (SD) fidelity to all elements of the diet protocol was 82 (18)%.

Adverse events

Physiotherapists were able to safely deliver the weight loss intervention as shown by no serious intervention-related adverse events, and no participant discontinuing the trial due to an adverse event (Table 5). A small number of participants reported non-serious adverse events in both groups. At 6 months, more Control participants reported taking pain medication and using co-interventions than in the Intervention group (Table 2).

Discussion

We found that the physiotherapists in this study were able to deliver a VLED alongside an exercise program that resulted in substantial weight loss, was safe and yielded high satisfaction in people with knee OA who had overweight or obesity. The mean weight loss in the Intervention group exceeded the desired 5% loss recommended by OA management guidelines [18] [17], with over a third achieving more than 10% loss at 6 months.

Comparison with other studies

To our knowledge, this is the first RCT to evaluate whether physiotherapists can safely and effectively deliver a dietary intervention with the aim of weight loss in any patient population. The magnitude of weight loss of participants in the Intervention group at six months (8.1% body weight) was comparable to other dietitian-delivered VLEDs in people with knee OA (8.7 % [39] 9.4% [38]), despite these studies having significantly greater therapist contact (26 [39] and 56 [38] dietitian sessions). While the aim of our intensive diet phase was 10% body-weight loss, only 37% of participants achieved this, which is less than other studies with more intensive VLED interventions with greater clinician support [38, 39]. Of note, the mean between-group difference in weight loss (7.5% body weight) in the present study is comparable to our previous RCT which included the same two treatment protocols but with the VLED delivered by dietitians (8.2% body weight loss) [18] and meal replacements being provided for substantially longer (26 weeks) [18].

Despite considerably greater weight loss in the Intervention group than Control, this was not reflected in better pain and function outcomes, with both groups showing clinically relevant improvements [42]. Diet plus exercise has previously been shown to provide slightly greater

improvements in self-reported pain and function compared to exercise alone in people with knee OA [18 39 43 38], with weight loss partially mediating this improvement [44]. However, the clinical significance of this supplementary benefit remains ambiguous [18 39 43].

Strengths and limitations

Strengths of this study include blinding of the assessor for the primary outcome, high level of participant retention and physiotherapist fidelity to the treatment protocols. Participant adherence to the dietary intervention protocol was generally good and comparable with our trial of the same VLED intervention but delivered by dietitians [18]. Only six physiotherapists delivered the intervention, so it may not be appropriate to generalise results to all physiotherapists. Given physiotherapists delivered both intervention arms, there is potential for contamination by greater focus on weight in control interactions. However, this would attenuate between-group differences. We did not include a follow-up period to assess weight loss maintenance, as this was not a study aim, and it is well known that weight is regained without ongoing support [45]. As no participants in the Control achieved ≥10% weight loss, sparse data may lead to biased estimates of the treatment effect [46]. Firth logistic regression was used to analyse this binary secondary outcome to minimise bias, however, we still observed wide 95% confidence intervals corresponding to risk ratio estimates [40]. Four participants self-reported body weight, a risk for measurement error bias, however sensitivity analysis excluding these participants yielded similar results.

Implications for clinical practice

The primary outcome of this study, together with safety and fidelity measures, provides evidence that physiotherapists can be upskilled to deliver a VLED intervention for people with knee OA with overweight or obesity. Future research could directly compare a physiotherapist-delivered VLED to a dietitian-delivered or self-managed VLED on weight loss outcomes and consider conversely if dietitians could be upskilled to deliver exercise alongside a VLED. Of the physiotherapists recruited, two thirds were relatively inexperienced in clinical practice (<five years), and none had previous weight management training. Our findings have potential relevance to healthcare settings where physiotherapists have similar professional standards to Australia, [47-49]. Further research is required to understand feasibility and costing approaches of training a larger group of physiotherapists in VLED delivery and including dietary support in routine physiotherapy clinical practice and existing or new care models.

Conclusion

A six-month VLED plus exercise intervention delivered by physiotherapists led to clinically significant substantial weight loss, was safe, and resulted in high levels of patient satisfaction compared to exercise alone for people with knee OA and overweight or obesity. This study provides the first evidence that with additional training, physiotherapists can effectively and safely deliver an intensive dietary weight loss program.

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Contributor Statement

KLB and KA obtained funding for the trial; KA, KLB and RSH designed the trial with input from SEJ, PS, JQ, FM, MH, NEF and ESG. SEJ, KA and KLB developed the training modules, and SEJ conducted the mock patient training, audited the practice patient training and provided training feedback to physiotherapists. SEJ and JP co-ordinated the trial. PL, ADS and KLB prepared the statistical analysis plan blinded and PL performed statistical analyses with guidance from ADS. KA and KLB wrote the draft of this paper and all authors edited and approved the final version.

Competing Interests

The authors have no competing interests to declare.

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Ethical Approval

The University of Melbourne Human Research Ethics Committee approved the study (HREC 1955042).

Availability of data and material

The datasets used and/or analysed during the current trial will be made available from the corresponding author on reasonable request.

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560 **Table 1. Diet intervention outline**
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Phase	Aim	Diet	Timing	Physiotherapy session principles & topics
Phase 1: Intensive weight loss via VLED	Weight loss of 5-10% body weight loss, replacing 2 meals per day with meal replacement products and a third low carbohydrate meal.	VLED (800 kcal (3280 kJ) per day with a carbohydrate intake of ≤ 50-60 g per day including 2 x meal replacements, 1 x meal of high protein, low carbohydrate consisting of protein, non-starchy vegetables or salad, and a tablespoon of oil/fat (if gall bladder in situ) per day) OR Modified VLED if participant unwilling to undergo VLED diet (number and frequency of meal replacements negotiated with participant) OR Healthy eating plan (if participant unwilling to undergo VLED or modified VLED).	Weeks 0-12 maximum (Physiotherapy sessions 1, 2, 3 +/- 4)	Session 1: Introduction and collaborative development of a tailored management plan including weight loss goals and weight loss target and information about the VLED diet. Sessions 2-3: Discuss progress and use motivational interviewing principles to help motivation, self-efficacy and to overcome barriers preventing participants completing their weight loss plan, progress and familiarize participants with their resource booklets. Specific topics and activities: • Portion sizes • Carbohydrates and glycaemic index • Supermarket shopping guide • Healthy snacks • Choosing a support person • If-Then Planning • Identifying eating triggers • Overcoming barriers to losing weight and keeping it off • Hunger level scale
Phase 2a: Transition of VLED diet onto healthy eating plan	Transition to 1 meal replacement per day and re-introduce low GI carbohydrates for one meal and maintain one low carbohydrate meal.	Transition to healthy eating plan including 1 x meal replacement, 1 x meal of high protein, low carbohydrate, 1 x meal of low GI carbohydrates +/- protein for two weeks.	Two-week period starting Week 13 OR when participant lost 10% body weight OR if participant was unwilling or wished to discontinue VLED diet *	Session 4: To discuss progress and use motivational interviewing principles to help motivation, self-efficacy and to overcome barriers preventing participants for the transition phase, progress and familiarize participants with their resource booklets. Specific topics and activities: • Transition and potential challenges and strategies • Healthy eating habits • Identifying eating habits • Changing thought patterns • Food diary

			(Physiotherapy session 4 or 5)	
<u>Phase 2b</u>: Healthy eating plan for weight maintenance	**AIM:** To adopt a healthy eating plan for weight maintenance.	Healthy eating plan of 3 meals per day including high protein, low glycaemic index carbohydrate, low fat foods consistent with the principles of the CSIRO total well-being diet	From end of transition to end of study at week 24 and beyond (Physiotherapy session 5 and/or 6)	<u>Session 5 & 6:</u> To discuss progress, discharge goals and considerations and use motivational interviewing principles to help motivation, self-efficacy and to overcome barriers to healthy eating phase, progress and familiarize participants with their resource booklets. Specific topics and activities: • Healthy eating progress • Managing food portions • Choosing low GI foods • Snacking • Food diary • Problem solving for adherence • Weight and food diaries • Relapse management and problem solving • Weight monitoring and considerations for returning to a VLED in future • Major barriers • Role of physical activity • Other options for multidisciplinary input

VLED = very low energy diet; GI = glycaemic index, CSIRO = Commonwealth Scientific and Industrial Research Organisation Total Well-being diet (29).
* Meal replacements were provided to participants free of charge for 14 weeks (12 weeks for the VLED diet and 2 for the transition). If a participant did not wish to transition off the VLED diet by 14 weeks or if they wanted to recommence the diet between weeks 14 and 24 they were required to purchase the meal replacement products at their own cost.

566 **Table 2. Baseline characteristics of participants by group.**

Baseline characteristic	Control (n=46)	Intervention (n=42)
Age, (years), mean (SD)	60.0 (8.3)	60.5 (7.0)
Female, n (%)	29 (63)	27 (64)
Height (m), mean (SD)	1.7 (0.1)	1.7 (0.1)
Weight (kg), mean (SD)	99.8 (18.0)	98.9 (15.0)
Body mass index (kg/m^2), mean (SD)	35.3 (5.3)	35.2 (5.3)
Highest education level, n (%)		
Completed primary school	5 (11)	3 (7)
Completed secondary school/high school	14 (30)	11 (26)
Completed university bachelor degree or higher	27 (59)	28 (67)
Currently employed, n (%)	30 (65)	34 (81)
Unilateral symptoms, n (%)	16 (35)	18 (43)
Knee symptom duration (years), median (IQR)	3.0 (1.0-10.0)	3.0 (1.0-8.0)
Number of other pain sites, median (IQR)	3.0 (2.0-5.0)	3.0 (2.0-5.0)
Comorbid conditions (self-reported), n (%)		
≥1 comorbid condition	30 (65)	27 (64)
Heart disease	1 (2)	4 (10)
High blood pressure	12 (26)	13 (31)
Depression	5 (11)	3 (7)
Diabetes	3 (7)	1 (2)
Spine condition	13 (28)	15 (36)
Lung disease	0 (0)	3 (7)
Cancer	4 (9)	1 (2)
Ulcer or stomach disease	0 (0)	1 (2)
Kidney disease	0 (0)	0 (0)
Liver disease	0 (0)	1 (2)
Anaemia or other blood disease	1 (2)	0 (0)
Treatments for knee in last 6 months, n (%)		
≥1 treatment	31 (67)	27 (64)
Massage	6 (13)	8 (19)
Gait aid	8 (17)	2 (5)
Education course	3 (7)	4 (10)
Land-based and water exercises	20 (44)	19 (45)
Joint injections	2 (4)	2 (5)
Acupuncture	4 (9)	3 (7)
Herbal therapies	8 (17)	6 (14)
Hot/cold treatment	15 (33)	13 (31)
Number of serious attempts to lose weight last 5 years, n (%)		

No attempts	5 (11)	6 (14)
1-2 attempts	20 (44)	22 (52)
3-10 attempts	17 (37)	13 (31)
10+ attempts	4 (9)	1 (2)
Current pain medication use, n (%) *		
≥1 medication used	25 (54)	27 (64)
Non-steroidal anti-inflammatory drugs	19 (41)	12 (29)
Acetaminophen	20 (44)	18 (43)
Topical anti-inflammatory drugs	11 (24)	9 (21)
Oral corticosteroids	0 (0)	0 (0)
Oral opioids	0 (0)	1 (2)
Expectation of treatment outcome, n (%)		
No effect at all	0 (0)	0 (0)
Minimal improvement	5 (11)	4 (10)
Moderate improvement	24 (53)	19 (45)
Large improvement	14 (31)	19 (45)
Complete recovery	2 (4)	0 (0)

SD=standard deviation; kg=kilograms; m=metres; IQR= interquartile range (25th to 75th percentile);
* Defined as ≥ 1 time per week over the last month for knee condition.

Table 3. Summary measures and estimated between-group mean differences (95% CI) for each outcome as appropriate using multiply imputed data

	Baseline [a] mean (SD)		6 months [a] mean (SD)		Within-group change [b] mean (SD)		Difference in change between groups [c] Intervention vs Control	
	Control N=46	Intervention N=42§	Control N=46‡	Intervention N=42‖	Control N=46	Intervention N=42	Mean (95% CI)	P-value
Primary outcome								
Percentage change in weight †#	N/A	N/A	1.0 (3.2)	8.1 (5.2)	1.0 (3.2)	8.1 (5.2)	7.2 (5.1, 9.3)	<0.001
Secondary outcomes								
Body mass index (kg/m^2) †	35.3 (5.3)	35.2 (5.3)	34.6 (4.6)	31.9 (5.3)	0.4 (1.2)	2.8 (1.7)	2.4 (1.7, 3.0)	<0.001
Waist circumference (cm) †	108.0 (11.1)	109.3 (11.2)	108.0 (10.2)	103.6 (12.4)	-0.7 (7.2)	5.4 (5.7)	5.8 (2.9, 8.7)	<0.001
Waist-to-hip ratio †	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.0, 0.0)	0.10
Knee pain walking (NRS) †	6.2 (1.3)	5.5 (1.2)	3.5 (2.2)	3.2 (1.8)	2.8 (2.2)	2.4 (1.9)	-0.1 (-1.0, 0.8)	0.82
Intermittent pain (iCOAP) †	12.0 (4.4)	12.5 (3.3)	6.1 (5.1)	4.9 (4.6)	5.8 (5.3)	7.5 (4.2)	1.4 (-0.6, 3.4)	0.17
Constant pain (iCOAP) †	8.7 (4.6)	9.1 (3.5)	5.9 (4.1)	5.3 (3.9)	2.6 (4.6)	3.6 (4.5)	0.6 (-1.1, 2.4)	0.48
Physical function (WOMAC) †	26.5 (11.4)	23.1 (10.9)	16.7 (14.0)	13.3 (9.5)	10.0 (11.0)	9.9 (13.3)	1.2 (-3.8, 6.2)	0.63
Quality-of-life (AQoL-6D) *	0.7 (0.2)	0.7 (0.1)	0.7 (0.2)	0.8 (0.1)	-0.1 (0.1)	-0.1 (0.1)	0.0 (-0.1, 0.0)	0.08
Physical activity (PASE) *	129.2 (82.8)	165.0 (87.8)	157.5 (77.6)	207.2 (121.9)	-33.9 (68.8)	-34.1 (80.6)	-1.4 (-37.2, 34.5)	0.94
Weight self-stigma (WSSQ) †	32.2 (8.8)	33.9 (8.8)	31.3 (7.7)	30.5 (9.7)	1.4 (5.8)	3.4 (7.5)	1.7 (-1.3, 4.8)	0.26

30 sec chair sit-to-stand (n) *	8.9 (2.7)	9.3 (2.9)	11.6 (3.6)	12.5 (3.2)	-3.0 (2.1)	-3.0 (2.6)	0.0 (-1.1, 1.1)	0.99
40m fast paced walk (sec) †	1.6 (0.3)	1.7 (0.4)	1.7 (0.3)	1.9 (0.4)	-0.2 (0.2)	-0.2 (0.3)	0.0 (-0.1, 0.1)	0.97
6-step stair climb (sec) †	9.9 (4.0)	9.5 (4.3)	7.9 (3.6)	7.0 (2.1)	2.3 (2.5)	2.2 (2.6)	0.0 (-1.1, 1.1)	0.98
Quadriceps strength (Nm/kg) *	1.2 (0.6)	1.3 (0.6)	1.4 (0.5)	1.6 (0.6)	-0.2 (0.2)	-0.3 (0.3)	-0.1 (-0.2, 0.0)	0.20

SD=standard deviation; CI=confidence interval; kg=kilogram; m=metre; cm=centimetre; n=number; sec=second; Nm=newton metre; NRS=numerical rating scale, 0-10 with higher scores indicating more pain; iCOAP=Intermittent and Constant Osteoarthritis Pain measure, 0-20 for constant pain subscale and 0-24 for intermittent pain subscale with higher scores indicating more pain; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index, 0-68 for physical function with higher scores indicating worse function AQoL-6D=Assessment of Quality-of-Life instrument-6 dimension, -0.04–1.00 with higher scores indicating better quality of life; PASE=Physical Activity Scale for the Elderly, 0-400+ with higher scores indicating greater levels of physical activity; WSSQ=Weight Self-Stigma Questionnaire, 12-60 with higher scores indicating greater internalized weight stigma

[a] Mean and standard deviation for baseline and 6-months are based on the available complete case data (observed data).

[b] Within-group change was calculated as baseline minus follow up for all outcomes based on the available complete case data (observed data), except primary outcome where the 6-month measure is the same as the within-group measure

[c] Difference in change between groups was adjusted for the outcome at baseline (except primary outcome where baseline weight was used) and the randomisation stratification variables of sex and physiotherapist

§ N=41 for 40m fast paced walk.

‡ N=42 for weight, body mass index, NRS, iCOAP intermittent pain, iCOAP constant pain, WOMAC, AQoL-6D, PASE, and WSSQ. N=36 for waist circumference, waist-to-hip ratio, 30 sec chair sit-to-stand, 40m fast paced walk, 6-step stair climb, and quadriceps strength.

|| N=38 for weight, body mass index, NRS, iCOAP intermittent pain, iCOAP constant pain, WOMAC, AQoL-6D, and WSSQ. N=37 for waist circumference, waist-to-hip ratio, PASE, 30 sec chair sit-to-stand, 40m fast paced walk, 6-step stair climb, and quadriceps strength.

* For change within groups, negative changes indicate improvement. For difference in change between groups, negative differences favour Diet+Exercise.

† For change within groups, positive changes indicate improvement. For difference in change between groups, positive differences favour Diet+Exercise.

Calculated as (baseline weight minus follow up weight/baseline weight) x 100

Table 4: Binary secondary outcomes and adjusted relative risks and risk differences.

	Control N=46 n/Total (%)	Intervention N=42 n/Total (%)	Relative Risk * (95% CI)	P-value	Risk Difference * (95% CI)	P-value
Global knee improvement[a,b]	20/42 (48)	27/38 (71)	1.5 (1.0, 2.0)	0.03	0.2 (0.0, 0.4)	0.02
Achieving ≥5% loss of body weight[c]	5/42 (12)	29/38 (76)	5.8 (2.7, 12.7)	<0.001	0.6 (0.5, 0.8)	<0.001
Achieving ≥10% loss of body weight[c, d]	0/42 (0)	14/38 (37)	24.79 (1.68, 366.04)	0.02	0.38 (0.23, 0.53)	<0.001

CI=confidence intervals

The counts and proportions are based on the available complete case data (observed data). The relative risks and risk differences are from models fit using multiply imputed data.

[a] Rated using a 7-point scale with terminal descriptors 'much worse' to 'much better', those indicating 'moderately better' or 'much better' classified as improved.

[b] Adjusting for randomisation stratification variables of sex and physiotherapist

[c] Adjusting for baseline weight and randomisation stratification variables of sex and physiotherapist

[d] Analysed using a Firth logistic regression model due to rare events

* Risk differences > 0 and relative risks > 1 favour Intervention

605 **Table 5. Adverse events, pain medications,other co-interventions and patient**
606 **adherence, fidelity and program satisfaction**
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Characteristic	Control N=46	Intervention N=42
Adverse events *		
Discontinued due to related adverse event, n (%)	0/42 (0%)	0/38 (0%)
Any serious adverse events, n (%) †	0/42 (0%)	0/38 (0%)
Number of non-serious related adverse events	6	3
Knee pain	1	0
Pain at other sites	5	2
Medical occurrence	0	1
Participants with non-serious related adverse events (self-reported), n(%)	5/42 (12%)	2/38 (5%)
Knee pain	1/42 (2%)	0/38 (0%)
Pain at other sites	4/42 (10%)	2/38 (5%)
Low blood pressure	0/42 (0%)	1/38 (3%)
Pain medication use ‡		
≥1 medication	21/42 (50%)	13/38 (34%)
Acetaminophen alone or in combined formulations	15/42 (36%)	10/38 (26%)
Topical anti-inflammatory drugs	8/42 (19%)	5/38 (13%)
Non-steroidal anti-inflammatory drugs	9/42 (21%)	3/38 (8%)
Oral glucocorticoids	1/42 (2%)	0/38 (0%)
Oral opioids	3/42 (7%)	1/38 (3%)
Other co-interventions §		
≥1 treatment	38/42 (90%)	27/38 (71%)
Stretching exercises	33/42 (79%)	22/38 (58%)
Hot/cold treatment	14/42 (33%)	10/38 (26%)
Education course	10/42 (24%)	9/38 (24%)
Hydrotherapy	9/42 (21%)	7/38 (18%)
Herbal therapies	7/42 (17%)	6/38 (16%)
Massage	5/42 (12%)	6/38 (16%)
Phone counselling	3/42 (7%)	7/38 (18%)
Aerobic exercise class	1/42 (2%)	5/38 (13%)
Participant adherence, fidelity, and program satisfaction		
Number of consultations attended (0-6) **	4.5 (1.9)	5.0 (1.2)
Duration of consultations (mins) **	24.8 (4.2)	51.3 (7.9)
Self-reported number of completed prescribed exercise sessions in past 2 weeks at 6 months (0-6) +	3.9 (2.0)	4.0 (1.8)
Percentage adherence to exercise sessions in past 2 weeks at 6 months+	64.7 (34.0)	66.7 (30.7)

Rating of adherence to exercise program (0-10) ^	6.5 (2.9)	7.3 (1.8)
Rating of adherence to physical activity plan (0-10) ^	6.3 (3.1)	7.5 (1.8)
Rating of adherence to diet program (0-10) ^	N/A	7.8 (1.8)
Number of weeks used meal replacements (0-24)	N/A	16 (6.4)
Number of participants who reported purchasing their own meal replacements beyond 14 weeks of funded replacements	N/A	22/37 (60%)
Satisfied with treatment program, n (%) †	26/42 (62%)	36/38 (95%)

Data are presented as mean (SD) for continuous measures and n/Total (%) for categorical measures based on complete data.

* Adverse events defined as any untoward medical occurrence in a participant that does not necessarily have a causal relationship with the treatment. Denominator varies depending on the number of participants who completed the adverse events section of the questionnaire in each group.

† Serious adverse events defined as any untoward medical occurrence that resulted in death, was life threatening, required hospitalisation, resulted in persistent or significant disability or incapacity, or any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed.

‡ Defined as taken at least once per week for their knee problem over the prior month.

§ Defined as having tried the co-intervention specifically for their knee pain or to reduce their body weight in the previous 24 weeks (but not including study interventions).

Self-reported adherence data Control N=42, Intervention= 38

** Control N=46, Intervention N= 42

[+] Control N=42, Intervention=37

^ Scored on an 11-point numeric rating score with higher scores indicating greater self-reported adherence

† Scored on a 7-point global rating of change scale with response options from “extremely dissatisfied” to “extremely satisfied” with participants indicating they are moderately or extremely satisfied deemed to be “satisfied” with the program

Figure 1. Flow chart describing progression of participants through the randomized controlled trial.

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