

# Is There a Dose-Response Relationship Between Weight Loss and Symptom Improvement in Persons With Knee Osteoarthritis?

INOSHI ATUKORALA,<sup>1</sup> JOANNA MAKOVEY,<sup>2</sup> LUKE LAWLER,<sup>3</sup> STEPHEN P. MESSIER,<sup>4</sup>  
KIM BENNELL,<sup>5</sup> AND DAVID J. HUNTER<sup>2</sup>

**Objective.** We examined the dose-response relationship between weight reduction and pain/functional improvement in persons with symptomatic knee osteoarthritis (KOA) participating in a community-based weight loss program.

**Methods.** Consecutive participants with KOA and enrolled in the 18-week Osteoarthritis Healthy Weight for Life weight-loss program were selected. In this completer-type analysis, participants were assessed at baseline, 6 weeks, and 18 weeks for body weight and Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales. The dose-response relationship between weight-change categories (>10%, 7.6–10%, 5.1–7.5%, 2.6–5.0%, and <2.5% of body weight loss) and change in KOOS scores was assessed by repeated-measures analysis of variance, controlling for sex and age, body mass index (BMI), and KOOS. The Western Ontario McMaster Universities Osteoarthritis Index function score derived from the KOOS was used to assess a meaningful clinical functional improvement.

**Results.** A total of 1,383 persons (71% females) were enrolled. Mean  $\pm$  SD age, height, and weight were  $64 \pm 8.7$  years,  $1.66 \pm 0.09$  meters, and  $95.1 \pm 17.2$  kg, respectively. Mean  $\pm$  SD BMI was  $34.4 \pm 5.2$  kg/m<sup>2</sup> with 82% of participants obese at baseline. A total of 1,304 persons (94%) achieved a >2.5% reduction in body weight. There was a significant dose-response relationship between all KOOS subscales and percentage of weight change across all weight-change categories. Participants required  $\geq 7.7\%$  (95% confidence interval 5.2, 13.3) body weight loss to achieve a minimal clinically important improvement in function.

**Conclusion.** There is a significant dose-response relationship between percentage of weight loss and symptomatic improvement. This study confirms the feasibility of weight loss as a therapeutic intervention in KOA in a community-based setting.

## INTRODUCTION

Symptomatic knee osteoarthritis (KOA) is the most common cause of lower extremity disability and diminished quality of life (1). Currently, there is no cure for this condition and contemporary management is limited to pain

relief and improvement in function by modification of risk factors of disease (2). Among risk factors currently identified, obesity is the single most important factor for development of severe KOA (3). As obesity is increasing in prevalence globally, particularly in the elderly, it is likely that more individuals will be affected by KOA in the future (4). Obesity is the leading risk factor for KOA incidence and, in addition, obesity contributes directly to the genesis of symptoms and to the need for joint replacement (5). This relationship is

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<sup>1</sup>Inoshi Atukorala, MD: University of Colombo, Colombo, Sri Lanka; <sup>2</sup>Joanna Makovey, MD, David J. Hunter, PhD: Royal North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, New South Wales, Australia; <sup>3</sup>Luke Lawler, BSc: Prima Health Solutions, Sydney, New South Wales, Australia; <sup>4</sup>Stephen P. Messier, PhD: Wake Forest University, Winston-Salem, North Carolina; <sup>5</sup>Kim Bennell, PhD: University of Melbourne, Melbourne, Victoria, Australia.

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Address correspondence to David J. Hunter, MD, Rheumatology Department, North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, New South Wales, Australia. E-mail: david.hunter@sydney.edu.au.

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## Significance & Innovations

- This is the first community-based study to demonstrate the dose-response relationship between weight reduction magnitude and reductions in pain and improvement in function in persons with symptomatic knee osteoarthritis (OA).
- A greater weight reduction is likely to cause incremental improvement in symptoms and function in knee OA.
- Those with higher levels of baseline function require less weight loss to achieve a clinically meaningful improvement in function.

driven in part by increased mechanical load; a single kilogram of body weight causes 4 kg of knee joint compression with each step (6).

Weight reduction has the ability to decrease the pain and disability associated with KOA. Previous meta-analyses conclude that a >5% reduction in weight will result in moderate-to-large improvements in self-reported disability (7). In addition, the pivotal Intensive Diet and Exercise for Arthritis (IDEA) trial identified a similar improvement with >40% reduction in symptoms in those losing >10% of their body weight (8). Therefore, greater reductions in weight are likely to lead to incremental improvements in knee joint loads with subsequently greater symptomatic benefits. Based on this evidence supporting its efficacy, weight management is advocated by most KOA guidelines (9). However, weight management is not frequently implemented in clinical practice (10). This phenomenon is attributed to patient difficulties in seeking health care, as well as to patients experiencing difficulties in adherence and engagement with recommended strategies. In addition, clinicians do not effectively promote weight loss in their patients (11). Despite several published trials of weight loss in persons with KOA, insufficient heed has been paid to community implementation and real-world effectiveness (12).

Although a greater weight loss is likely to lead to greater symptom improvement, a clear dose-response relationship has not been established in KOA outside the tightly controlled confines of a clinical trial. The intent of this investigation is to examine whether there is a relationship between the magnitude of weight reduction and the magnitude of pain and functional improvement in persons with symptomatic KOA in a real-world, community-based setting. This study also explores the feasibility of achieving weight loss in a less-controlled community setting.

## MATERIALS AND METHODS

Participants were persons with symptomatic KOA consecutively enrolled in a specialized knee and hip OA management program that focuses on weight loss, i.e., the Osteoarthritis Healthy Weight For Life Program (OAHWFL). The OAHWFL program is implemented by Prima Health Solutions Pty Ltd, a quality certified health care organization (AS/NZS ISO

9001:2008) in Australia and New Zealand. The program is run on behalf of participating health funds and its full cost (including meal replacements) is borne by the insurance/health care fund. The OAHWFL program systematically implements a number of core nonsurgical OA best practice treatment recommendations (13), including targeting >5% weight loss for overweight individuals, land- and water-based aerobic exercise (walking and swimming), muscle strengthening, and self-management and education strategies.

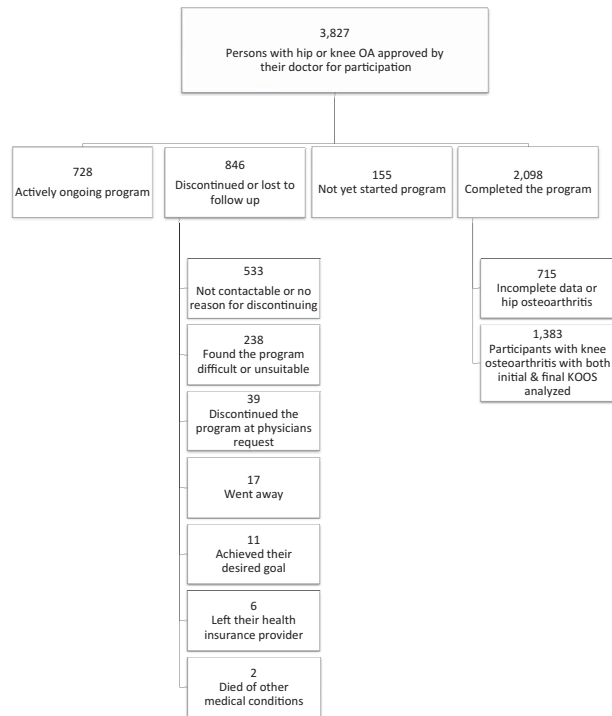
This program utilizes a step-by-step approach that consists of 3 phases, carried out over 18 weeks. Each 6-week phase includes a portion control eating plan (including KicStart very low calorie diet meal replacements); an activity plan and physiotherapist-developed strength, balance, and mobility exercises; a personalized online symptom, progress, and satisfaction tracking (phone and mail alternatives also available) activity; and 2-way personal motivation, support, and advice via phone, short message service/text message, e-mail, message board, and mail.

**Study sample.** The study was conducted in Australia with participants from both rural and urban settings. All participants in the OAHWFL program fulfilled the 1986 American College of Rheumatology clinical criteria for classification of KOA (14). Participants had a current or historical diagnosis of KOA supported by radiology (e.g., on radiographs or magnetic resonance imaging) or by an incidental finding from a previous arthroscopy and a body mass index (BMI) >28 kg/m<sup>2</sup>. In addition, all participants had, according to medical opinion, KOA symptoms that required (or were likely to in the foreseeable future) referral to an orthopedic surgeon for evaluation for a knee joint replacement procedure. In these persons' weight loss, improved fitness and muscle strength prior to surgery was desirable.

Consecutive persons enrolled in the OAHWFL program and fulfilling the eligibility criteria were selected. The primary process of enrollment for OAHWFL was as follows (Figure 1). Individuals ages ≥50 years identified by hospital claims data as having undergone a minor surgical knee procedure (such as arthroscopy) indicative of KOA were mailed a detailed explanation of OAHWFL (with invitation to join the program) by their private health insurance provider. Those choosing to enroll in the program were then required to obtain a written referral from their general practitioner, orthopedic surgeon, or rheumatologist confirming their weight and height and radiographic or arthroscopic diagnosis of KOA. Strict radiologic criteria were not used in the diagnosis. The participant demographics are shown in Table 1.

Ethics approval was obtained from the Health and Research Ethics Committee of the Northern Sydney Local Health District.

**Intervention.** The aim of this web-based program was to achieve a weight loss of 7–10% by gradually changing dietary habits over 18 weeks. The initial 6-week motivational weight-loss program was followed by a consolidation phase and a short-term maintenance phase, each lasting 6 weeks. This 18-week program was followed by an open-ended, long-term maintenance phase. The interventional structure of this online dietary control and



**Figure 1.** Outline of participant selection for the analysis. OA = osteoarthritis; KOOS = Knee Injury and Osteoarthritis Outcome Score.

behavior modification program is described in the phases below (Figure 2).

*Phase 1: 6-weeks, motivational weight loss.* Participants were instructed to consume a nutritionally complete, very low calorie, diet meal replacement (KicStart), a food supplement developed specifically for medical purposes of

weight loss by Prima Health Solutions Pty Ltd. KicStart was consumed for 2 meals per day in combination with controlled portions and “free foods” (e.g., berries and leafy greens). This initial motivational phase was designed to result in early weight loss and improve motivation and adherence (15).

*Phase 2: 6-weeks, consolidation weight loss.* One meal replacement per day, “free foods,” and portion-controlled lunch and dinner were used to progressively wean participants off the meal replacements.

*Phase 3: 6-weeks, short-term weight maintenance.* Portion-controlled whole foods for breakfast, lunch, and dinner with “free foods.”

During the open-ended long-term maintenance period, participants were advised to take portion-controlled whole foods for all meals with “free foods.”

Throughout the program, participants were given a choice of KicStart meal replacement flavors. In addition, all were provided with access to recipes for low-fat and low-glycemic index meals. They were encouraged to maintain adequate hydration using free drinks (e.g., mineral water, vegetable juice). Online healthy eating and lifestyle education was provided, as was personalized telephone motivation, support, and advice at predetermined intervals and on demand. Body weight and waist circumference diaries were completed (online) every 2 weeks by participants. If any potential safety concerns were identified, the participants were referred back to their general practitioner. The dietary program used in these patients with KOA was modeled on a similar dietary program that included KicStart for rapid weight loss in other conditions. This program was proven to be effective in obese or overweight persons with type 2 diabetes mellitus, obese women undergoing fertility treatment, and in weight reduction in atrial fibrillation management (16–18).

**Outcomes.** All participants were assessed at baseline, 6, and 18 weeks. Body weight and height was self-reported, though initial weight and height was confirmed by each participant’s general practitioner. BMI was computed using this information. The exposure variable assessed was the proportion of body weight lost (%) from baseline to the weight assessed at 18 weeks of followup.

The Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire was assessed in all participants. The KOOS contains 42 items and takes approximately 10 minutes to self-administer. It comprehensively assesses 5 domains: pain (9 items), other symptoms (7 items), function in daily living (17 items), function in sports and recreation (5 items), and knee-related quality of life (4 items), with each section scored separately. A 5-point Likert scale is used and all items have 5 possible answer options scored from 0 (no problems) to 4 (extreme problems). Thereafter, a published algorithm was used to transform the scores to a 0–100 scale with 0 and 100 representing extreme knee problems and no knee problems, respectively. The KOOS has proven validity, reliability, and responsiveness in this population (19–21). The co-primary outcomes for this analysis were the KOOS subscales of pain, other symptoms, function in daily living, function in sports and recreation, and knee-related quality of life. The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) function score was derived from the

**Table 1. Demographic and clinical characteristics of the study participants at baseline\***

Baseline characteristics	Overall (n = 1,383)
Age, years	64.0 ± 8.7
Females, no. (%)	981 (70.9)
Weight, kg	95.12 ± 17.2
Height, meters	1.66 ± 0.09
BMI, kg/m <sup>2</sup>	34.39 ± 5.17
Obesity (BMI ≥30 kg/m <sup>2</sup> ) at baseline, no. (%)	1,130 (81.7)
Obesity (BMI ≥30 kg/m <sup>2</sup> ) at 18 weeks, no. (%)	772 (56.3)
Baseline KOOS pain subscale	56.3 ± 16.8
Baseline KOOS function in daily living subscale	59.5 ± 18.3
Baseline KOOS other symptoms subscale	54.3 ± 17.7
Baseline KOOS function in sport/recreation subscale	27.6 ± 24.2
KOOS knee related quality of life subscale	35.1 ± 18.4

\* Values are the mean ± SD unless indicated otherwise. BMI = body mass index; KOOS = Knee Injury and Osteoarthritis Outcome Score.



Figure 2. The 3-phase interventional structure of the Healthy Weight for Life online dietary control and behavior-modification program.

KOOS. A higher score in the WOMAC scale indicates a higher degree of functional impairment.

**Statistical analysis.** The dose-response relationship between weight-change categories (<2.5% weight loss, 2.5–5.0%, 5.1–7.5%, 7.6–10%, and >10%) and change in each KOOS domain was assessed using a repeated-measures analysis of covariance, controlling for sex, baseline age, baseline KOOS, and baseline BMI. The weight-loss categories were based on the IDEA trial goal (≥10%), the weight-loss goal of the diet groups in the Arthritis, Diet and Activity Promotion study (5%), and the weight loss typically achieved in an exercise-only cohort of older adults with KOA (<5%) (22). Regression analysis was performed with

models adjusted for age, sex, baseline weight, and baseline KOOS measures. The minimal clinically important improvement (MCII) in WOMAC function was identified using the criteria developed by Tubach et al (23). These criteria take into account that the MCII is affected by the initial severity of symptoms. An absolute change of 5.3, 11.8, and 20.5 in the WOMAC function score is required for an MCII in those who start with low, intermediate, and high baseline WOMAC scores, respectively.

**RESULTS**

At the time of analysis, 3,827 persons with knee or hip OA were approved by their doctor for participation in

**Table 2. Relationship between the different weight loss categories (according to percentage body weight loss) and KOOS subscales\***

	Body weight loss						Significance (linearity)
	All (n = 1,383)	≤2.5% (n = 79)	2.5–5% (n = 224)	5–7.5% (n = 332)	7.5–10% (n = 317)	≥10% (n = 431)	
Difference in weight (kg) from baseline	-7.9 ± 4.2	-1.3 ± 1.0	-3.8 ± 1.0	-5.9 ± 1.3	-8.2 ± 1.6	-12.5 ± 3.5	0.000
Age, years	64.0	63.3	63.9	63.8	64.7	63.9	0.557
Baseline weight	95.1 ± 17.2	95.8 ± 20.8	96.1 ± 17.9	94.3 ± 16.9	94.3 ± 17.4	95.7 ± 16.1	0.881
Baseline KOOS pain	56.3 ± 16.8	58.2 ± 18.2	54.4 ± 15.9	57.6 ± 16.9	56.5 ± 17.0	55.9 ± 16.7	0.813
Difference in KOOS pain subscale after weight loss	13.1 ± 16.3	6.1 ± 13.0	9.9 ± 16.8	12.0 ± 17.1	13.3 ± 15.1	16.7 ± 16.1	0.000
Baseline KOOS function in daily living (WOMAC function score)	59.5 ± 18.3	59.2 ± 19.1	57.1 ± 17.5	61.5 ± 17.7	59.9 ± 18.9	59.1 ± 18.6	0.687
Difference in KOOS function in daily living subscale (WOMAC function score) after weight loss	13.3 ± 16.1	7.8 ± 13.3	8.9 ± 14.7	12.0 ± 16.7	13.6 ± 15.5	17.4 ± 16.3	0.000
Baseline KOOS symptoms	54.3 ± 17.6	53.8 ± 18.7	54.4 ± 17.7	55.2 ± 17.3	54.1 ± 18.3	53.8 ± 17.3	0.580
Difference in KOOS symptoms subscale after weight loss	12.5 ± 15.9	7.8 ± 14.6	8.6 ± 15.3	11.9 ± 16.1	11.7 ± 14.9	16.4 ± 16.2	0.000
Baseline KOOS function in sport	27.6 ± 24.2	27.5 ± 26.3	25.5 ± 22.8	29.2 ± 24.1	26.7 ± 24.8	28.1 ± 24.0	0.550
Difference in KOOS function in sport subscale after weight loss	12.6 ± 24.8	5.9 ± 26.7	9.0 ± 22.3	11.5 ± 25.1	12.7 ± 24.6	16.4 ± 25.1	0.000
Baseline KOOS knee-related quality of life	35.1 ± 18.4	35.6 ± 20.0	33.8 ± 18.9	35.8 ± 17.5	35.3 ± 18.2	35.1 ± 18.9	0.777
Difference in KOOS quality of life subscale after weight loss	12.7 ± 18.2	5.3 ± 17.6	9.9 ± 17.1	12.4 ± 18.6	12.0 ± 17.7	16.2 ± 18.2	0.000

\* Values are the mean ± SD unless indicated otherwise. A positive difference for the Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales indicates an improvement. WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

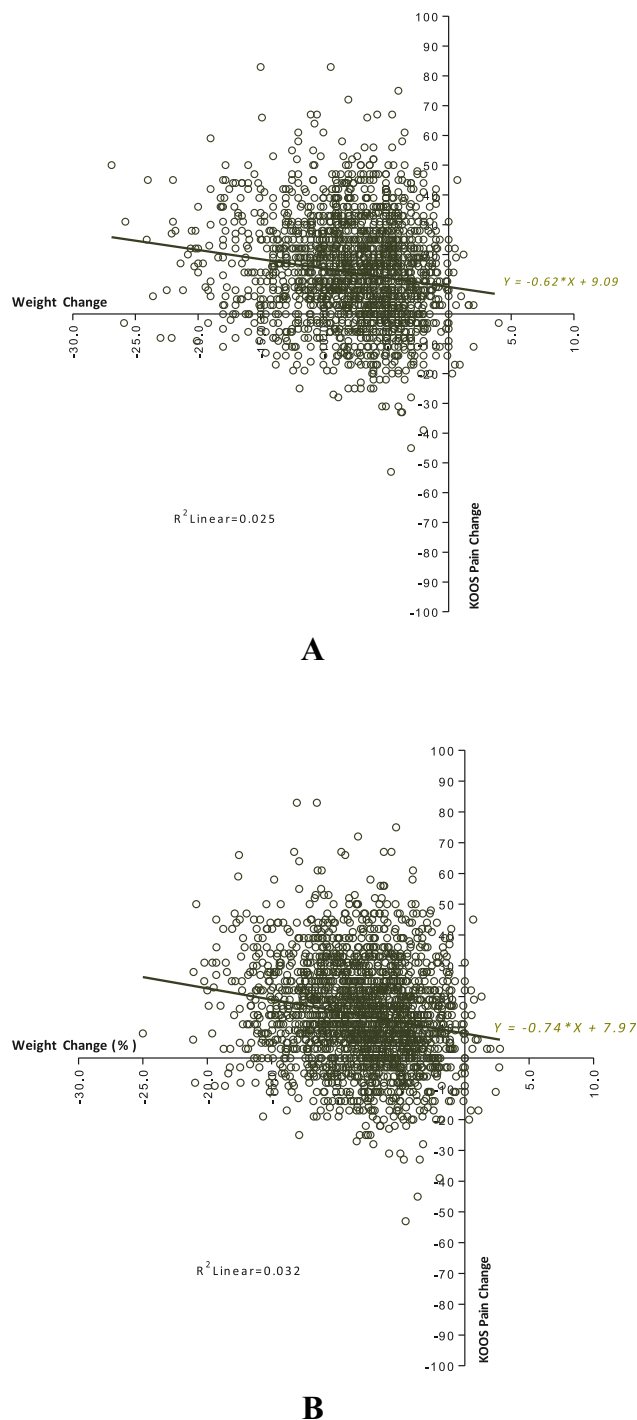
OAHWFL (Figure 1). Of these, 155 had not yet started the program, 728 were actively undertaking the program, and 846 had discontinued or were lost to followup. Of the 2,098 who completed the program, 715 were excluded from analysis because of incomplete data or OA of the hip. Therefore, 1,383 participants (70.9% female) were included in this study.

The mean ± SD weight of this cohort was 95.1 ± 17.2 kg, with an average height of 1.66 ± 0.09 meters. The majority was obese with a mean ± SD BMI of 34.4 ± 5.2 kg/m<sup>2</sup>. The mean ± SD KOOS pain, other symptoms, function in daily living, function in sports and recreation, and knee-related quality of life subscale scores at baseline were 56.3 ± 16.8, 54.3 ± 17.7, 59.5 ± 18.3, 27.6 ± 24.2, and 35.1 ± 18.4, respectively (Table 1).

During the study period, 1,304 participants (94.2%) had a >2.5% reduction in body weight. The mean ± SD weight loss of all groups was 7.9 ± 4.2 kg with a weight loss of 8.3% of baseline body weight. The number (%) of participants according to percentage weight loss categories were as follows: <2.5% category: 79 (5.7); 2.6–5% category: 224 (16.2); 5.1–7.5% category: 332 (24.0); 7.6–10% category: 317 (22.9), and >10% category: 431 (31.2). The mean ± SD

absolute weight loss across the categories was as follows: <2.5% category: 1.3 ± 1.0 kg; 2.5–5% category: 3.8 ± 1.0 kg; 5.1–7.5% category: 5.9 ± 1.3 kg; 7.6–10% category: 8.2 ± 1.6 kg, and >10% category: 12.5 ± 3.5 kg. Participants in the different weight-loss categories did not differ on sex, age, or baseline KOOS measures (Table 2).

There was a significant dose-response relationship between change in each of the KOOS subscales and percentage of weight change across all weight change categories (Table 2). This association persisted in regression models adjusted for age, sex, baseline weight, and baseline KOOS measures (Figure 3). The group with the largest amount of weight loss (≥10% body weight loss) showed the greatest improvement in pain, function, and other domains assessed. All participants required at least 7.7% body weight loss to achieve an MCII in the WOMAC function score. An MCII in WOMAC function was achieved (an absolute score improvement of 9.1) in those participants achieving at least a 7.7% (95% confidence interval [95% CI] 5.2, 13.3) weight loss. Participants with a lower baseline function in the WOMAC score (i.e., a lesser level of functional impairment) required 6.9% (95% CI 4.96, 8.87) body weight loss. Those with a higher level of functional impair-



**Figure 3.** Regression plots of weight change (in kg [A] and as a percentage [B]) against Knee Injury and Osteoarthritis Outcome Score (KOOS) pain change.

ment at baseline required a higher percentage of body weight loss to achieve an MCII in function (Table 3).

## DISCUSSION

This study established a clear dose-response relationship between weight loss and symptom improvement in over-

weight and obese people with KOA undergoing a standardized weight-loss program in a community setting. It demonstrates that weight loss is feasible in this setting, with the majority of participants having lost a significant amount of weight over the 18 weeks, and nearly one-third achieving more than 10% weight loss. Weight loss in the study group was associated with a significant improvement in pain and function, with the improvement in pain/function demonstrated across the different weight-loss groups. However, a greater than 10% body weight loss was associated with greater improvement in KOOS subscales when compared to the lowest weight-loss group (2.5–5% body weight loss). Importantly, we have defined the amount of weight loss needed for a clinically meaningful improvement in WOMAC function. A percentage weight loss of at least 7.7% was required for an MCII. Those with lower levels of function at baseline were required to lose at least 10% of their body weight to achieve an MCII, while those with a better level of function at baseline required a lesser amount of weight loss for an MCII. These findings emphasize the importance of weight loss in improving symptoms and function in overweight/obese persons with KOA.

Obesity is associated with poor functional outcome in KOA (24,25). This is in part due to the adverse mechanical effects and in part due to obesity-related inflammation (26). The mechanical effects of increasing BMI on knee compression forces alter balance, muscle strength, and gait (27). In fact, previous research has shown increased body weight in KOA causes an increased absolute peak ground reaction force during walking (28). The visceral and subcutaneous truncal white adipose tissue secretes cytokines and adipokines such as interleukin-1 (IL-1), leptin, and adiponectin into the systemic circulation. These cytokines and adipokines are increased in obesity and laboratory studies have implicated obesity-related inflammation with the occurrence of KOA (29–31). Increased IL-1 $\beta$ , a cytokine that is elevated in obesity, is associated with higher rates of OA (32) and increased pain in knee OA (33). Similarly, adiponectin is involved in key pathways of inflammation and matrix degradation in the human joint (34). Leptin promotes the synthesis of transforming growth factor (TGF)  $\beta$  (the human joint TGF form) that in turn, stimulates osteophyte formation and impairs cartilage repair (35). It has been shown that the serum adiponectin/leptin ratio is a predictor of OA pain (36). Weight loss is associated with reduction in these inflammatory adipokines (37). Furthermore, it is postulated that reduction in serum leptin is one mechanism by which weight loss improves physical function and symptoms in OA patients (38).

Weight loss reduces knee joint loading and peak knee compressive forces (8) known to be associated with pain (39). This too could account for the improvement in symptoms. Synovial inflammation contributes to severe pain in KOA and weight loss reduces inflammatory markers TGF $\beta$ , IL-1 $\beta$ , and tumor necrosis factor  $\alpha$  (40). Greater reduction in IL-6 levels and knee compressive forces was demonstrated in the combined diet and exercise group than in the exercise group of the IDEA clinical trial (7). Therefore, it is intuitive that weight loss will improve the symptoms of knee OA, and this fact has been established in high-quality randomized controlled trials (7,8,22) and by a meta-

**Table 3. Regression analysis of the MCII score of WOMAC function score absolute change and percentage of weight loss in all study participants and low, intermediate, and high baseline score tertiles\***

WOMAC function score (0–100) absolute change	No.	Unadjusted $\beta$ (95% CI)	<i>P</i>	Adjusted $\beta$ (95% CI)†	<i>P</i>
All participants, MCII –9.1	1,383	–7.58 (–9.46, –5.70)		–7.73 (–13.26, –5.20)	< 0.0001
Low baseline score tertile, MCII –5.3	450	–6.91 (–8.89, –4.93)	< 0.0001	–6.92 (–8.87, –4.96)	< 0.0001
Intermediate baseline score tertile, MCII –11.8	453	–8.47 (–12.49, –4.44)	< 0.0001	–9.23 (–13.26, –5.20)	< 0.0001
High baseline score tertile, MCII –20.4	450	–9.28 (–14.96, –3.61)	< 0.0001	–10.05 (–15.43, –4.67)	< 0.0001

\* MCII = minimum clinically important improvement; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; 95% CI = 95% confidence interval. A higher WOMAC score indicates a higher degree of functional impairment.  
† Models adjusted for age, sex, baseline weight, and baseline WOMAC function score.

analysis that showed weight loss in KOA patients was associated with significantly reduced disability (7). This meta-analysis highlighted that a weight loss of at least 10% would result in a moderate-to-large clinical effect. Low-calorie diets cause symptom improvement in KOA (8,41). These trials have demonstrated the superiority of combined diet and exercise over weight loss by exercise alone in improving knee OA symptoms (8,22). Therefore, there is adequate evidence supporting the effectiveness of weight loss intervention in knee OA, particularly by diet.

However, at this point, evidence for the efficacy of weight loss intervention in knee OA has been established mainly by randomized clinical trials, conducted under strictly controlled settings with intensive person-to-person contact. This study is unique in that it demonstrates the feasibility of dietary intervention, coupled with motivational support, in a true-to-life community setting. It is noteworthy that the entire dietary intervention was supported by remotely delivered interventions, which were web-, paper-, or telephone-based. In addition, this project demonstrated the effectiveness of focusing on weight loss per se in improving knee OA symptoms. This study demonstrated a dose-response relationship between weight-loss categories and pain, other symptoms, function in daily living, function in sports and recreation, and knee-related quality of life. The dose-response relationship persisted in models corrected for baseline age, sex, BMI, weight, and height, confirming the dose-response relationship of weight loss in symptom improvement in knee OA across all the KOOS subscales. The fact that the benefit is seen in similar magnitude across all KOOS subscales suggests that weight loss confers general benefits across a range of KOA symptoms rather than having a differential effect. The fact that lower levels of weight loss caused clinically meaningful improvement in function in those with better baseline function shows the usefulness of weight loss in all persons with KOA, even if they have good baseline function.

However, this study has limitations. The main shortcoming is the absence of a control group. This shortcoming could not be rectified as this study relied on retrospective assessment of data collected on patients enrolled with the specific purpose of weight loss. In addition to a dietary weight-loss component, this program included strength/balance/mobility exercise, personal support, and pain management strategies as other interventions. We were not able to evaluate the effects of these other program components on the outcomes

and it is possible that these contributed to the improvement seen in the low weight-loss group. It is assumed that the effects of these other interventions were consistent across the cohort and therefore would not have influenced the dose-response relationships noted for weight loss. Another limitation is that the study relied on self-reported weight assessment. However, previous studies have shown that self-reported weight correlates well with measured weight loss, and it is unlikely that any error associated with self-reported assessment was systematic across weight loss categories (42). Another limitation is that data were available only for persons currently participating in the program or for those who had just completed the program. A proportion had discontinued the program. This can introduce bias or perhaps an overestimation of the effects. It would also be preferable to ascertain the effect of the weight loss at a longer time point following completion of the program. As this information was not available, we cannot comment on the sustainability of weight loss achieved from this program. In addition, there was no information on the socioeconomic status of the study population. While this does not alter the findings of the study, we are unable to determine whether weight loss of clinically meaningful amounts can be achieved by individuals of different socioeconomic levels.

In conclusion, this study established the dose-related symptomatic response to weight reduction in people with knee OA in a community setting. It also demonstrates that a clinically relevant improvement in symptoms can be achieved with a relatively modest weight loss. The study is novel in that it demarcates the different amounts of weight loss required for those with different levels of function at baseline. These cutoffs are useful in setting weight-loss targets for patients in clinical practice. It is encouraging that weight reduction, through a remotely delivered mode of instruction, is feasible in the community setting and can achieve weight loss magnitudes conducive to benefits in pain, function, and a range of other patient outcomes. Given the dose-response noted, individuals should be advised that even small amounts of weight loss could be beneficial, but that greater benefits can be obtained with increasing amounts of weight loss. Further dissemination of weight loss strategies is warranted to address the burgeoning risk factor of obesity in persons with knee OA. Further studies utilizing a control group in addition to the weight-loss group and assessing the magnitude of contribution of the exercise programs to weight loss are recommended. Assessing the cost effectiveness of weight-loss strategy in

KOA would be useful in establishing the place of this useful intervention in the management of KOA.

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## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Hunter had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Atukorala, Messier, Bennell, Hunter.

**Acquisition of data.** Lawler, Hunter.

**Analysis and interpretation of data.** Atukorala, Makovey, Messier, Bennell, Hunter.

## ADDITIONAL DISCLOSURE

Author Lawler is the CEO and Scientific Director of Prima Health Solutions, which delivers the Healthy Weight for Life program. There is no commercial or financial relationship with any of the other investigators.

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