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Weight loss: the treatment of choice for knee osteoarthritis? A randomized trial

R. Christensen M.Sc.†‡, Prof. A. Astrup D.M.Sc., M.D.‡ and Prof. H. Bliddal D.M.Sc., M.D.†*

† *The Parker Institute, H:S Frederiksberg Hospital, Denmark*

‡ *The Department of Human Nutrition, The Royal Veterinary and Agricultural University, Frederiksberg, Denmark*

Summary

Objective: We wanted to assess the effect of rapid diet-induced weight loss on the function of obese, knee osteoarthritis (OA) patients.

Methods: Eighty patients with knee OA, 89% women ($n = 71$), were recruited. Mean (SD) body-mass index (BMI) was 35.9 (5.1) kg/m^2 and age 62.6 (11.1) years. Patients were randomized to either a low-energy diet (LED 3.4 MJ/day), or a control diet (5 MJ/day). The LED group had weekly dietary sessions, whereas the control group was given a booklet describing weight loss practices. Changes in body weight and body composition were examined as independent predictors of changes in knee OA symptoms. Symptoms were monitored by the Western Ontario and McMaster Universities' (WOMAC) OA index.

Results: The LED and control group lost a mean (SE) of 11.1 (0.6)% and 4.3 (0.6)%, respectively, with a mean difference being 6.8% (95% confidence interval (CI): 5.5 to 8.1%; $P < 0.0001$). The decrease in body fat percent was higher in the LED group, 2.2% (1.5 to 3.0%; $P < 0.0001$). The total WOMAC index improved in the LED group ($P < 0.0001$), but not in the control group ($P = 0.12$), mean difference: −219.3 mm (−369.2 to −69.4 mm; $P = 0.005$). The 'Number Needed to Treat (NNT)' to ensure an improvement in WOMAC $\geq$ 50% was 3.4 (2.1 to 8.8) patients. Changes in total WOMAC index were best predicted by the reduction of body fat percent, with a 9.4% (4.8 to 13.9%) improvement in WOMAC for each percent of body fat reduced ($P = 0.0005$).

Conclusions: In our patients with knee OA, a weight reduction of 10% improved function by 28%. LED might be of advantage to control diet because of the rapidity of weight loss and a more significant loss of body fat.

Key words: Knee osteoarthritis, Weight loss, Diet, Obesity, Musculoskeletal, Pain, Physical function, Rehabilitation.

Introduction

Osteoarthritis (OA) is a major cause of morbidity and disability among the elderly, affecting—as it does—approximately 70% of population over 65 years of age[1]. Knee OA is accompanied by both pain and loss of function, both of which are of crucial importance for social competency[2]. Non-surgical therapy of knee OA often focuses on a pharmacological approach and includes analgesic agents or non-steroidal anti-inflammatory drugs (NSAIDs)[3]. This type of therapy may imply serious health hazards because of adverse gastrointestinal effects[4,5]. Overweight, and especially obese, persons run a high risk of OA in the knee and probably also the hips and hands, although the mechanism by which obesity causes OA is poorly understood[6]. Lifestyle changes are gaining increasing recognition in the management of OA, and stepping up advice on the importance of increased physical therapy and weight reduction is increasingly being recommended[7]. At present, there is no consensus as to the benefits provided by weight loss in obese patients with knee OA[8], or whether weight loss has to be in combination with increased physical fitness[3]. However, reduced body weight will be beneficial for OA patients in several ways[9–14], including a reduced load on the weight-bearing joints[6,15]. There is an indication that the reduction in body fat, rather than body weight overall, may be the best predictor for improvement of OA symptoms in the knee[16].

We conducted a randomized, controlled trial to quantify how much pain relief and increased physical function elderly obese patients with knee OA would have, following an intensive 8-week dietary weight loss intervention.

* Address correspondence and reprints to: Professor Henning Bliddal, The Parker Institute, Frederiksberg Hospital, DK-2000 F Denmark. Tel: 45-38164151; Fax: 45-38164159.; E-mail: henning.bliddal@fh.hosp.dk

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Methods

STUDY DESIGN AND SELECTION OF PATIENTS

After approval by the local ethical committee, patients were recruited from the outpatient clinic of the Department of Rheumatology, H:S Frederiksberg Hospital, Denmark. Overweight patients over 18 years of age, with primary knee OA, diagnosed according to the American College of Rheumatology[17] were considered eligible for the trial. All our patients had radiographic severity grade 2 or 3 on the Kellgren and Lawrence scale[18]. Major exclusion criteria were: history or active presence of other rheumatic diseases that might be responsible for secondary OA, and diabetes mellitus, as well as other endocrine disorders. Likewise, substantial abnormalities in hematological, hepatic, renal or cardiac functions would exclude a participant from

enrollment. The patients had to be overweight as defined by body-mass index (BMI) > 28 kg/m^2. Only patients who explicitly expressed a clear, unequivocal motivation for weight loss and who were fluent in Danish, were invited to participate. Before inclusion in the study, fasting blood glucose was measured as well as hemoglobin and TSH. The participants were asked not to change medication during the 8-week period of the study.

TREATMENT ASSIGNMENT

All the subjects were randomly assigned to either 8 weeks of low-energy diet (LED; 3.4 MJ/day) or an 8-week conventional hypo-energetic, high protein diet (app. 5 MJ/day)—defined as a control group. For every 16 patients included, randomization was done in a stratified way, according to gender, BMI and age—ensuring homogeneity between intervention groups.

The LED consisted of nutrition powder (Speasy®, Dansk Droge A/S) dissolved in water and was taken as six daily meals, giving the patient 3.4 MJ/day. This met all the recommendations for a daily intake of high quality protein[19]; 37 energy percent (E%) from protein (soy protein) providing the essential amino acids, 47 E% from carbohydrate, 16 E% from vegetable fat (primarily from rapeseed oil), and fibers from oat-bran (15 g/day). The LED group received nutritional instruction and behavioral therapy, by the same experienced dietician, at weekly sessions (1.5 h/week) throughout the 8 weeks—to reinforce and continuously stimulate the patients' decision about weight reduction, and to encourage a high degree of compliance.

Subjects receiving the conventional diet attended a thorough presentation, by the same dietician who treated the LED group, that gave nutritional advice in a 2-h session at baseline, and recommending ordinary foods in amounts, which would provide the patients with approximately 5 MJ/day. After this initial tutoring, all the patients in the hypo-energetic group received ideas for diet plans in a booklet providing the participants with a wealth of 'good-advice' on trying to reduce body weight. Thus, the patients assigned to the conventional hypo-energetic diet, were used as a control group, as there was no contact with the dietician after the dietary consultation at baseline.

OUTCOME MEASURES

The changes in body weight and body composition were examined as independent predictors of changes in the symptoms of knee OA. At baseline and after 8 weeks intervention body weights of all patients' were measured on a decimal scale (TANITA BWB-600S, 'Frederiksberg Vægtfabrik', Copenhagen, Denmark). Body composition was estimated by the bioimpedance method with an animeter (HTS-engineering, Odense, Denmark), and fat-free mass and fat mass were calculated with Danish standard equations[20]. Dual-energy X-ray (DXA) measures were obtained from all the patients at baseline (Norland DXA XR-36) and used for more precise characterization[21].

Symptoms of OA, as perceived by patients prior to the assessment, were monitored by the Western Ontario and McMaster Universities' (WOMAC) OA index, a validated, disease-specific questionnaire addressing the severity of joint pain (five questions), stiffness (two questions), and limitation of physical function (17 questions). The visual analogue scale (VAS) version of the index was used, with the patient assessing each question on a 100 mm VAS. The global 3-dimensional total WOMAC index was calculated by the summation of all 24 components, with 2400 mm being the worst possible score[22,23].

Furthermore, the index of Lequesne was applied, which is a Likert scale that also adds a 3-dimensional approach to the severity of the knee OA[24,25]. Finally, the Health Assessment Questionnaire (HAQ) was used to investigate the patients' disability[26].

SAMPLE SIZE AND STATISTICAL ANALYSIS

We wanted to detect a significant effect-size (ES $= |\mu_I - \mu_C|/\sigma) \geq 0.8$, which indicates a large effect compared to a proper placebo, whereas an ES < 0.2 is considered small and ES > 0.5 is moderate[8,27,28]. An expected ES ≥ 0.8 seemed reasonable, at least according to the study, based on a controlled clinical trial, by Huang *et al.*[29] who reported results from a dietary intervention equivalent to an ES of 1.8 (analyzed via difference in Lequesne Index) after an arithmetic mean weight loss between groups of 9.7 kg. We set $\alpha = 5\%$ and with a power $(1 - \beta)$ of 90% and a desired ES of 0.8, we calculated the sample size as 34 knee OA patients in each of the two groups[30]. For practical reasons, 16 participants were included at a time and we increased the sample size to 48 patients per group to allow a dropout rate of more than one in four. If the dropout rate is equal between the groups, and the missing data at follow-up (8 weeks) is missing at random, the risk of making a type I error is independent of 'last observation carried forward' bias[31]. All changes in clinical outcomes were analyzed as the difference from baseline $(X_8 - X_0)$, and the percentage change from baseline (calculated from the ratio: X_8/X_0). Data were analyzed using a two-factor analysis of covariance, with a factor for treatment and a factor for gender, using the baseline value as covariate to reduce the random variation[32], and increase power[33]. Unless stated otherwise, results are expressed as the difference between the final group means and 95% confidence interval (CI) with the associated *P* values, based on the General Linear Model (GLM) procedure[34]. To determine clinical efficiency, which we based on the relief of symptoms, we calculated the Number Needed to Treat (NNT)[35,36]. For the individual participant, a clinically significant improvement ('treatment') was defined as a reduction in WOMAC index $\geq 50\%$; extrapolated from the recommendations for pain measures[37]. To explore the best predictors of reduction in total WOMAC index, we used a stepwise linear-regression analysis with a no-intercept statement applied, with percentage change from baseline as response. All tests for homogeneity in the discrete data were analyzed using a χ^2-test, with a Yates correction. The SAS® statistical package (version 8; SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

Results

PATIENT CHARACTERISTICS

A total of 109 patients were screened prior to the enrollment of 96 participants in the study and they were randomly assigned to receive LED or a conventional hypo-energetic control diet. The 13 subjects, who were not enrolled in the study, were excluded for the following reasons: three patients had a BMI < 28 kg/m^2; two had hypothyroidism; one patient had previously undergone operation in both knees; seven patients decided to withdraw their consent before randomization and without further explanation. After the random allocation of 48 subjects to

each group, four patients in the LED group and three patients in the control group decided, before entering the study, to withdraw without further explanation. During the study, three patients in the LED group withdrew because of non-compliance with the intervention-regime and one decided to have a sub-acute knee replacement and did not turn up for therapy. In the control group, three withdrew due to lack of motivation, one due to a broken arm and one was excluded due to the diagnosis of type 2 diabetes mellitus. The following analyses are based on completers only, because of group similarity according to the low percentage of dropouts in the LED and control group, 4/44 (9%) and 5/45 (11%), respectively ($\chi^2_{Yates} = 0.001$; $P = 0.97$). Patients in the two groups had similar demographic and baseline characteristics (Table I). The average knee OA patient completing this trial was a 60-year-old woman, with a BMI of 36 kg/m^2, representing 20 kg of excess body weight. Patients had a moderate OA according to WOMAC and Lequesne Index and were well functioning apart from their knee OA as indicated by the HAQ.

WEIGHT AND BODY COMPOSITION OUTCOMES

Table II shows the outcomes after 8 weeks intervention. There was a significant weight reduction in both groups, while the LED group showed a significantly higher effect on body weight ($P < 0.0001$) than the control group, with a mean difference being 6.8 percentage points (5.5 to 8.1%) and 6.6 kg (5.3 to 7.9 kg). The change in body composition was more favorable in the LED than in the control group, e.g., the percentage of body fat decreased the most after LED, with a mean difference being 2.2 percentage points (1.5 to 3.0%; $P < 0.0001$). The proportion of patients who achieved more than 5% weight reduction in the LED and control group was: 92.5% and 25%, respectively ($\chi^2_{Yates} = 34.9$; $P < 0.0001$). Whereas the percentage of patients achieving >10% weight loss was 50% and 0%, respectively ($\chi^2_{Yates} = 24.1$; $P < 0.0001$), which corresponds to an NNT = 2 (1.5 to 2.9) patients.

EFFICACY RESULTS

There was an improvement in the primary symptom outcome measure represented by the total WOMAC index (Table II) compared with baseline in the patients receiving LED ($P < 0.0001$), whereas there was no significant effect after the control diet ($P = 0.12$) with a significant difference between the final group means, ES = 0.65 [0.20 to 1.10] ($P = 0.005$). The group receiving LED showed a highly significant improvement in the WOMAC-assessed function-score ($P < 0.0001$). There was no corresponding improvement in this score for those on the control diet ($P = 0.10$). Thus, LED resulted in a significant improvement in the WOMAC-assessed function-score compared to the reduction produced by the control diet, ES = 0.69 [0.24 to 1.14] ($P = 0.003$). There was a significant improvement in the WOMAC-assessed pain-score within the LED group ($P = 0.001$), whereas no effect was seen after the control diet ($P = 0.10$). However, this difference was of no significance when the groups were compared after the intervention (ES = 0.33 [−0.11 to 0.77]; $P = 0.15$). Likewise, there was a significant improvement in the WOMAC-assessed stiffness-score within the LED group ($P = 0.002$), whereas no effect was seen after the control diet ($P = 0.17$) and with no difference between the groups (ES = 0.36 [−0.08 to 0.80], $P = 0.11$). The Lequesne Index showed no significant effect of the intervention, neither within the LED group ($P = 0.06$) nor between the groups (ES = 0.12 [−0.32 to 0.56]; $P = 0.59$).

Table I
Baseline characteristics of participants by randomization group

Characteristics	Mean (SD)		
	Low-energy diet ($n_l = 40$; 3.4 MJ/day)	Control ($n_C = 40$; app. 5 MJ/day)	Total ($n = 80$; range)
Women, no. (%)	35 (88%)	36 (90%)	71 (89%)
Age (years)	60.5 (11.6)	64.6 (10.4)	62.6 (11.1) (35 to 90)
Body-mass index (kg/m^2)	36.3 (5.6)	35.5 (4.6)	35.9 (5.1) (28.8 to 55.1)
Weight (kg)	96.4 (15.5)	97.1 (13.4)	96.8 (14.4) (66.4 to 142.8)
Lean body mass (kg)†	43.9 (10.4)	43.3 (8.3)	43.6 (9.4) (30.0 to 70.3)
Fat mass (kg)†	47.6 (11.9)	49.7 (10.2)	48.6 (11.1) (27.6 to 85.3)
Bone mineral content (kg)†	2.867 (0.402)	2.985 (0.389)	2.926 (0.398) (2.284 to 3.998)
Fat (%)†	50.4 (8.0)	51.7 (6.4)	51.0 (7.2) (27.3 to 63.3)
Bone mineral density (g/cm^2)†	1.054 (0.110)	1.096 (0.166)	1.075 (0.141) (0.878 to1.804)
Fat-free mass (kg)‡	50.6 (9.0)	51.1 (8.3)	50.9 (8.6) (34.0 to 76.7)
Plasma glucose (mmol/L)	5.9 (1.1)	5.8 (0.7)	5.8 (0.9) (4.3 to 10.2)
C-reactive protein (mg/L)§	3.8 (2.4; 6.5)	3.4 (2.1; 7.9)	3.5 (2.1; 7.2) (0.5 to 27.5)
Health assessment questionnaire, score§	0.4 (0.2; 0.9)	0.4 (0.2; 0.6)	0.4 (0.2; 0.8) (0 to 1.8)
Lequesne Index, total (score)	12.7 (4.3)	12.7 (4.4)	12.7 (4.3) (0 to 21)
WOMAC index‖			
Total index (mm)	950.1 (455.8)	838.2 (546.8)	894.1 (503.3) (0 to 2101)
Pain (mm)	197.0 (96.0)	170.5 (115.7)	183.7 (106.5) (0 to 469)
Function (mm)	678.9 (338.0)	592.1 (399.8)	635.5 (370.4) (0 to 1440)
Stiffness (mm)	74.5 (50.0)	75.1 (55.2)	74.8 (52.3) (0 to 189)

†Assessed using Dual-energy X-ray (Norland DXA XR-36).

‡Assessed using bioimpedance (HTS-engineering, Odense, Denmark), significantly different from the sum of lean body mass and bone mineral content 4.4 kg (95% CI: 3.6 to 5.1 kg; $P < 0.0001$).

§Showed a non-gaussian distribution, thus, presented as median (interquartile range).

‖Sum of visual analogue scale scores.

Table II
Change in outcomes from baseline after 8 weeks in knee OA patients who completed either the intensive low-energy diet (Speasy®) or a conventional dietetic regime (Control)

Characteristics	Mean (SE)		Difference (95% CI)	*P* value
	Low-energy diet ($n_I = 40$; 3.4 MJ/day)	Control ($n_C = 40$; app. 5 MJ/day)		
Weight loss (%)	11.1 (0.6)	4.3 (0.6)	6.8 (5.5 to 8.1)	<0.0001
ΔWeight (kg)	−11.0 (0.6)	−4.4 (0.6)	−6.6 (−7.9 to −5.3)	<0.0001
ΔFat-free mass (kg)†	−3.0 (0.4)	−1.2 (0.4)	−1.8 (−2.4 to −1.1)	<0.0001
ΔFat mass (kg)†	−7.7 (0.5)	−2.9 (0.5)	−4.8 (−5.9 to −3.8)	<0.0001
ΔFat (%)†	−3.3 (0.3)	−1.0 (0.4)	−2.2 (−3.0 to −1.5)	<0.0001
ΔLequesne Index, total (score)	−1.4 (0.8)	−1.0 (0.8)	−0.4 (−2.1 to 1.2)	0.59
Change in WOMAC index‡				
ΔTotal index (mm)§	−334.5 (69.1)	−115.2 (72.4)	−219.3 (−369.2 to −69.4)	0.005
ΔPain (mm)§	−57.0 (16.9)	−29.8 (17.7)	−27.2 (−64.0 to 9.7)	0.15
ΔFunction (mm)§	−252.5 (49.6)	−85.6 (51.9)	−166.9 (−274.5 to −59.3)	0.003
ΔStiffness (mm)§	−22.6 (7.2)	−10.2 (7.4)	−12.4 (−27.7 to 2.8)	0.11

†Assessed using bioimpedance (HTS-engineering, Odense, Denmark).
‡Sum of visual analogue scale scores.
§Two patients in the control group did not provide answers for the WOMAC questionnaire after 8 weeks ($n_C = 38$).

Based on those subjects, who showed more than 50% reduction in the total WOMAC index after LED compared to the control diet, the NNT was 3.4 (95% CI: 2.1 to 8.8). Thus, more than 25% of obese patients with knee OA will experience a clinically significant improvement in daily functional activities after an 8-week period with LED.

When testing to what extent the individual changes in body composition (and body weight) could predict %changes in total WOMAC index, the best predictor was the change in the percentage of body fat ($P = 0.0001$). The change in body fat (expressed as percentage points) explained as much as 18% of the variation in %WOMAC ($R^2 = 0.179$; $P = 0.0001$); with an effect-slope, $\beta = 9.4$%WOMAC per body-fat percentage point (95% CI: 4.8 to 13.9%WOMAC per body-fat percentage point); Fig. 1(a). In comparison, the %reduction in body weight predicted 15% of the variation in %WOMAC ($R^2 = 0.146$; $P = 0.0005$); with an effect-slope, $\beta = 2.8$%WOMAC per %body-weight (95% CI: 1.3 to 4.3%WOMAC per %body-weight); Fig. 1(b). When analyzing %changes in total WOMAC index in a multivariate regression analysis model, using the change in body fat (percentage point) and %weight loss as independent predictors, neither of the variables stays below the predefined significance level ($\alpha = 0.05$), $P > 0.07$; and the model does not add more information about the variability ($R^2 = 0.180$).

Discussion

The present study demonstrates that a highly significant increase in the function of obese patients with knee OA may be obtained by an intervention consisting of simple weight reduction. The typical patient in our clinic is an elderly woman, significantly overweight, and trapped in a negative pattern of continual weight gains and pain, accompanied in turn, by decreasing activity and functional capacity.

We, like others, have conducted rather extensive training programs with elderly, knee OA patients[38] and during these activities it has been our definite impression that obesity has been a key factor behind the troubles of this group. While training in principle is good, it will increase the wear-and-tear of the diseased joint and some indications of adverse effects of training have been found[38]. Likewise, reduction of pain may in some cases lead to accelerated joint destruction, although this tends to be more pronounced with the use of certain NSAIDs[39,40]. By contrast, a weight reduction would not be expected to induce any untoward effect for the patient, provided the intervention ensures a sufficient supplement of vitamins and essential nutrients[19,41]. In our study, this was accomplished by employing a highly enriched dietary supplement[42], which enabled the patients to lose an optimum of 1.5 kg per week. Epidemiological evidence strongly supports the notion of excess weight being an important factor in the development of knee OA, with a decrease in risk of 50% after a reduction in BMI of more than 2 units (app. 5.1 kg) over a period of 10 years[15]; it is quite logical to assume that weight loss will be of benefit to patients with OA[43,44]. Our results seem to confirm indications of such an effect of weight loss in OA[16,29,44–48].

We found a highly significant association between increase in function and the reduction in the percentage of body fat, as 18% of the variation in the total WOMAC index change could be explained by the reduction in the percentage of body fat, with a change of 9.4%WOMAC per %body-fat. The weight loss alone predicted 15% of the variation, with a change of 2.8%WOMAC per %body-weight. These results are in accordance with a preliminary observation of body composition being a better predictor of change in the symptoms of knee OA, than body weight itself[16]. In rough figures, our results indicated that a 10% weight reduction would result in 28% decline in knee OA trouble. A moderate weight loss of 10% has important implications for obese persons in general[10,13]. In the present study the NNT (based on a 10% weight loss criterion) was 2 (95% CI: 1.5 to 2.9), whereas the NNT calculated on the basis of ≥ 50% reduction in total WOMAC was four patients.

The western world faces an obesity problem of vast dimensions. Obesity and diabetes are major causes of morbidity and mortality in the United States[49,50], as in the rest of the world. Body weight increases with age up to about 60 and then levels off[51]. At present, there is no consensus on the subject of elderly and ideal body weight and its association with mortality and morbidity[52]. However,

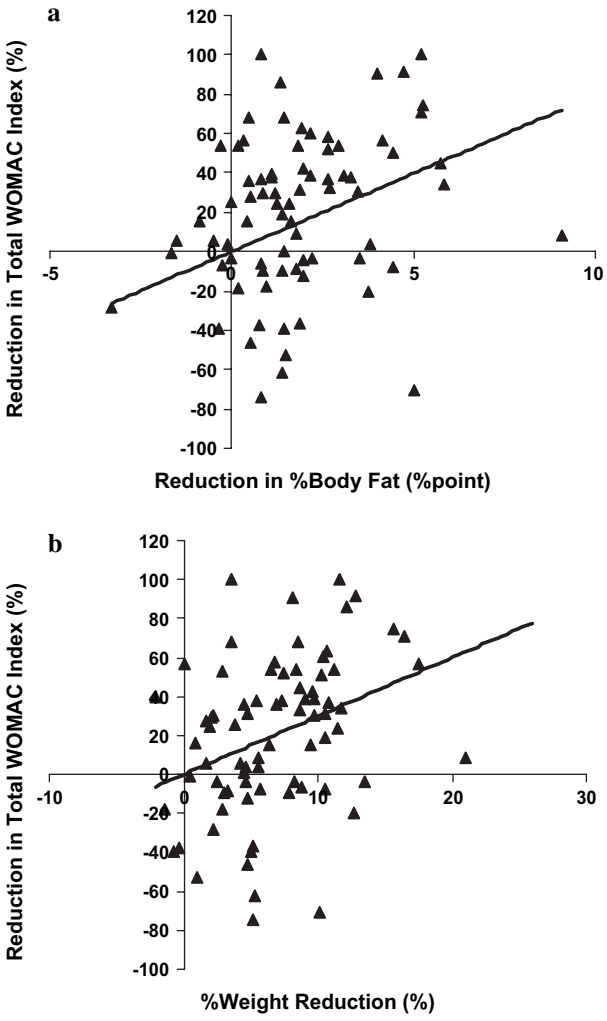

Fig. 1. Scatter plot showing the individual patients expressed as percentage change in total WOMAC index from baseline, following a weight loss regime, $n = 78$ patients. a: Reduction in total WOMAC index vs the reduction in body fat (%point). With a highly significant effect-slope, $\beta = 9.4\%$WOMAC per body fat %point (95% CI: 4.8 to 13.9; $P = 0.0001$). b: Reduction in total WOMAC index vs the percent reduction in body weight, $\beta = 2.8\%$WOMAC per %weight reduction (95% CI: 1.3 to 4.3; $P = 0.0005$).

based on the cross-sectional and cohort studies published, it seems reasonable to assume that weight loss in obese elderly people can reduce morbidity from diabetes and cardiovascular diseases[51,53]. In the case of type 2 diabetes, a reduction of the incidence may be obtained by the recommendation of a daily physical activity level (PAL) above 1.8[54]. 'The Finnish Diabetes Prevention Study' randomized 522 overweight subjects with impaired glucose tolerance to either lifestyle intervention or a control group. They found that applying counseling in both weight reduction (3.5 kg after 2 years) and increased physical activity in high-risk subjects, reduced the risk of diabetes by 58% at follow-up after 3.2 years[55,56]. If we combine the quantity of weight lost in this study, with the observed increment in physical function and ability for the majority of these patients, it may be speculated that their PAL was increased as well.

Overweight knee OA patients' insulin levels are statistically higher than in matched obese subjects without OA[57]. The insulin level (and insulin resistance) is the factor most strongly associated with diabetes incidence[58,59] and conversion to a healthier lifestyle may prevent the majority of new cases of type 2 diabetes[60].

Our results were obtained after a rather short intervention of 8 weeks, which lies well within the waiting-list interval for a knee operation in our district. An improvement in function due to weight loss is of interest for many patients and might be regarded as an alternative to knee replacement. Bachmeier *et al.* studied the outcomes in elderly OA patients undergoing total hip ($n = 86$) or knee ($n = 108$) replacement–the first year after surgery[61]. Based on their 3 month-results, we extracted and calculated the arithmetic mean %change in total WOMAC index and found a 36% reduction. In comparison, based on the mean values (presented in Tables I and II), our results show a reduction in total WOMAC index equivalent to 35% after 8 weeks intervention with LED. With equipotent results, weight loss might be advocated in the case of obese patients before a knee replacement is considered. The possible influence on the decision whether to operate or not may depend on many factors and should be tested in a controlled setting.

The patients had a 1-h personal interview with the dietician before and after the 8-week period of once-weekly team therapy, i.e., the total time spent per patient was 3.5 h. Add to this the daily cost of about 10 US dollars, which is the average price of Speasy® LED nutrition powder. Taken over 56 days, as a substitute for all other meals, the total cost for the outpatient clinic will thus be far less than 1000 US dollars for the entire 8-week period, which is considerably cheaper than most other treatment alternatives in OA[62]. The number of visits in the intervention group was high compared with the control group. The effect of attention in this group of patients will have to be taken into account; however, the considerable weight reduction in the intervention group could not have been obtained without the support of the dietician or the other participants in the group. Our control group had a trend towards an effect on pain just by entering the study. While not being of significance *per se*, this effect meant that the difference in the intervention group could only be shown in comparison with baseline and not as a treatment effect. This might be due to a type II error, as an ES = 0.3 would require 176 patients in each group, with a statistical power ($1 - \beta$) of 80%, to detect a significant difference ($\alpha = 5\%$) between the two groups[30].

The present 8 week intervention cannot go it alone, and the program must include a follow-up to stabilize weight. A general dogma among laymen and professionals is that rapid weight loss will result in a bad long-term maintenance. However, the lesson from obesity management programs shows that greater initial weight loss is associated with better long-term prognoses[63,64]. It is evident that substantial weight loss results in a reduced resting metabolic rate (RMR)[65], and that formerly obese subjects had a 3–5% lower mean relative RMR than control subjects[66]. However, there is no evidence to suggest that the rate of weight loss achieved by very LEDs is associated with any detriment to body composition or metabolic rate[67]. Accordingly, obese (knee OA) individuals should not let undue concerns about the hazards of weight cycling deter them from efforts to control their body weight[68]. As a further motivating factor, the increase in function of our patients with knee OA is very valuable and has a high impact on the health-related quality of life[48]. It is not known exactly how much functional impairment in these patients is due to overweight as compared with the joint disease *per se*. However, with the limited possibilities of medical therapy of the joint, the most effective non-surgical intervention is diet, both with regard

to increase in function and rapidity of the result. In comparison, the symptom relief in knee OA patients, associated with taking glucosamine sulfate for 3 years, is only 24%[69].

In conclusion, we found that an 8-week program with a 10% weight loss gave a highly significant increase in function in obese patients with knee OA. As the patients show a corresponding reduction in their risk of other health problems as well, weight loss is proposed as a first-choice therapy for knee OA.

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References

1. Bagge E, Bjelle A, Eden S, Svanborg A. Osteoarthritis in the elderly: clinical and radiological findings in 79 and 85 year olds. Ann Rheum Dis 1991;50:535–9.
2. Badley EM, Tennant A. Changing profile of joint disorders with age: findings from a postal survey of the population of Calderdale, West Yorkshire, United Kingdom. Ann Rheum Dis 1992;51:366–71.
3. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000;43: 1905–15.
4. Laine L. Gastrointestinal effects of NSAIDs and coxibs. J Pain Symptom Manage 2003;25:S32–40.
5. Deeks JJ, Smith LA, Bradley MD. Efficacy, tolerability, and upper gastrointestinal safety of celecoxib for treatment of osteoarthritis and rheumatoid arthritis: systematic review of randomised controlled trials. BMJ 2002;325:619.
6. Felson DT. Weight and osteoarthritis. Am J Clin Nutr 1996;63:430S–2S.
7. O'Reilly S, Doherty M. Lifestyle changes in the management of osteoarthritis. Best Pract Res Clin Rheumatol 2001;15:559–68.
8. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, *et al*. EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2003;62:1145–55.
9. Marckmann P, Toubro S, Astrup A. Sustained improvement in blood lipids, coagulation, and fibrinolysis after major weight loss in obese subjects. Eur J Clin Nutr 1998;52:329–33.
10. Goldstein DJ. Beneficial health effects of modest weight loss. Int J Obes Relat Metab Disord 1992;16:397–415.
11. Ziccardi P, Nappo F, Giugliano G, Esposito K, Marfella R, Cioffi M, *et al*. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. Circulation 2002;105:804–9.
12. Bastard JP, Jardel C, Bruckert E, Blondy P, Capeau J, Laville M, *et al*. Elevated levels of interleukin 6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. J Clin Endocrinol Metab 2000;85:3338–42.
13. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr 1992;56:320–8.
14. Anderson JW, Konz EC. Obesity and disease management: effects of weight loss on comorbid conditions. Obes Res 2001;9(Suppl 4):326S–34S.
15. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. The Framingham Study. Ann Intern Med 1992;116:535–9.
16. 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: 2181–6.
17. Altman RD. Criteria for classification of clinical osteoarthritis. J Rheumatol Suppl 1991;27:10–2.
18. Altman R, Brandt K, Hochberg M, Moskowitz R, Bellamy N, Bloch DA, *et al*. Design and conduct of clinical trials in patients with osteoarthritis: recommendations from a task force of the Osteoarthritis Research Society. Results from a workshop. Osteoarthritis Cartilage 1996;4:217–43.
19. National Task Force on the Prevention and Treatment of Obesity. Very low-calorie diets. National Task Force on the Prevention and Treatment of Obesity, National Institutes of Health. JAMA 1993; 270:967–74.
20. Heitmann BL. Prediction of body water and fat in adult Danes from measurement of electrical impedance. A validation study. Int J Obes 1990;14:789–802.
21. Tagliabue A, Andreoli A, Comelli M, Bertoli S, Testolin G, Oriani G, *et al*. Prediction of lean body mass from multifrequency segmental impedance: influence of adiposity. Acta Diabetol 2001;38:93–7.
22. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833–40.
23. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Rheum 2001;45:453–61.
24. Lequesne MG, Mery C, Samson M, Marty M. Comparison between the WOMAC and the Lequesne indices in patients with knee and hip osteoarthritis. Osteoarthritis Cartilage 1998;6:441–2.
25. Theiler R, Sangha O, Schaeren S, Michel BA, Tyndall A, Dick W, *et al*. Superior responsiveness of the pain and function sections of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) as compared to the Lequesne-Algofunctional Index in patients with osteoarthritis of the lower extremities. Osteoarthritis Cartilage 1999;7:515–9.
26. Memel DS, Kirwan JR, Langley C, Hewlett S, Hehir M. Prediction of successful application for disability benefits for people with arthritis using the Health Assessment Questionnaire. Rheumatology (Oxford) 2002;41:100–2.

27. Laird NM, Mosteller F. Some statistical methods for combining experimental results. Int J Technol Assess Health Care 1990;6:5–30.
28. McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. JAMA 2000;1469–75.
29. Huang M-H, Chen C-H, Chen T-W, Weng M-C, Wang W-T, Wang Y-L. The effects of weight reduction on the rehabilitation of patients with knee osteoarthritis and obesity. Arthritis Care Res 2000;13:398–405.
30. Campbell MJ, Julious SA, Altman DG. Estimating sample sizes for binary, ordered categorical, and continuous outcomes in two group comparisons. BMJ 1995;311:1145–8.
31. Gadbury GL, Coffey CS, Allison DB. Modern statistical methods for handling missing repeated measurements in obesity trial data: beyond LOCF. Obes Rev 2003;4: 175–84.
32. Vickers AJ, Altman DG. Statistics notes: analysing controlled trials with baseline and follow up measurements. BMJ 2001;323:1123–4.
33. Glueck DH, Muller KE. Adjusting power for a baseline covariate in linear models. Stat Med 2003;22: 2535–51.
34. SAS Institute Inc. 2nd edn. SAS/STAT User's Guide (GLM-VARCOMP) 1989;Volume 6:Cary, NC: SAS Institute Inc. 893–1673 pp.
35. Osiri M, Suarez-Almazor ME, Wells GA, Robinson V, Tugwell P. Number needed to treat (NNT): implication in rheumatology clinical practice. Ann Rheum Dis 2003;62:316–21.
36. Altman DG. Confidence intervals for the number needed to treat. BMJ 1998;317:1309–12.
37. McQuay HJ, Moore RA, Eccleston C, Morley S, Williams AC. Systematic review of outpatient services for chronic pain control. Health Technol Assess 1997; 1:1–135.
38. Rogind H, Bibow-Nielsen B, Jensen B, Moller HC, Frimodt-Moller H, Bliddal H. The effects of a physical training program on patients with osteoarthritis of the knees. Arch Phys Med Rehabil 1998;79: 1421–7.
39. Rashad S, Revell P, Hemingway A, Low F, Rainsford K, Walker F. Effect of non-steroidal anti-inflammatory drugs on the course of osteoarthritis. Lancet 1989;2: 519–22.
40. Huskisson EC, Berry H, Gishen P, Jubb RW, Whitehead J. Effects of antiinflammatory drugs on the progression of osteoarthritis of the knee. LINK Study Group. Longitudinal Investigation of Nonsteroidal Antiinflammatory Drugs in Knee Osteoarthritis. J Rheumatol 1995;22:1941–6.
41. Astrup A. Dietary approaches to reducing body weight. Baillieres Best Pract Res Clin Endocrinol Metab 1999; 13:109–20.
42. Eisenstein J, Roberts SB, Dallal G, Saltzman E. High-protein weight-loss diets: are they safe and do they work? A review of the experimental and epidemiologic data. Nutr Rev 2002;60:189–200.
43. McGoey BV, Deitel M, Saplys RJ, Kliman ME. Effect of weight loss on musculoskeletal pain in the morbidly obese. J Bone Joint Surg Br 1990;72:322–3.
44. Martin K, Nicklas BJ, Bunyard LB, Tretter LD, Dennis KE, Goldberg AP, *et al*. Weight loss and walking improve symptoms of knee osteoarthritis (OA). (Abstract)Arthritis Rheum 1996;39:225S.
45. Williams RA, Foulsham BM. Weight reduction in osteoarthritis using phentermine. Practitioner 1981; 225:231–2.
46. Messier SP, Loeser RF, Mitchell MN, Valle G, Morgan TP, Rejeski WJ, *et al*. Exercise and weight loss in obese older adults with knee osteoarthritis: a preliminary study. J Am Geriatr Soc 2000;48:1062–72.
47. Toda Y. The effect of energy restriction, walking, and exercise on lower extremity lean body mass in obese women with osteoarthritis of the knee. J Orthop Sci 2001;6:148–54.
48. 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;21:419–26.
49. Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, *et al*. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA 2003;289:76–9.
50. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–7.
51. Elia M. Obesity in the elderly. Obes Res 2001; 9(Suppl 4):244S–8S.
52. Rossner S. Obesity in the elderly—a future matter of concern? Obes Rev 2001;2:183–8.
53. Astrup A, Finer N. Redefining type 2 diabetes: 'diabesity' or 'obesity dependent diabetes mellitus'? Obes Rev 2000;1:57–9.
54. Astrup A. Healthy lifestyles in Europe: prevention of obesity and type II diabetes by diet and physical activity. Public Health Nutr 2001;4:499–515.
55. Lindstrom J, Eriksson JG, Valle TT, Aunola S, Cepaitis Z, Hakumaki M, *et al*. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish diabetes prevention study: results from a randomized clinical trial. J Am Soc Nephrol 2003;14: S108–13.
56. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, *et al*. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.
57. Silveri F, Brecciaroli D, Argentati F, Cervini C. Serum levels of insulin in overweight patients with osteoarthritis of the knee. J Rheumatol 1994;21:1899–902.
58. Hanson RL, Imperatore G, Bennett PH, Knowler WC. Components of the ''metabolic syndrome'' and incidence of type 2 diabetes. Diabetes 2002;51: 3120–7.
59. Mudaliar S, Edelman SV. Insulin therapy in type 2 diabetes. Endocrinol Metab Clin North Am 2001;30: 935–82.
60. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, *et al*. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med 2001;345: 790–7.
61. Bachmeier CJ, March LM, Cross MJ, Lapsley HM, Tribe KL, Courtenay BG, *et al*. A comparison of outcomes in osteoarthritis patients undergoing total hip and knee replacement surgery. Osteoarthritis Cartilage 2001;9:137–46.
62. Macario A, McCoy M. The pharmacy cost of delivering postoperative analgesia to patients undergoing joint replacement surgery. J Pain 2003;4:22–8.
63. Toubro S, Astrup A. Randomised comparison of diets for maintaining obese subjects' weight after major

weight loss: ad lib, low fat, high carbohydrate diet v fixed energy intake. BMJ 1997;314:29–34.
64. Astrup A, Rossner S. Lessons from obesity management programmes: greater initial weight loss improves long-term maintenance. Obes Rev 2000;1:17–9.
65. Garrow JS, Webster JD. Effects on weight and metabolic rate of obese women of a 3.4 MJ (800 kcal) diet. Lancet 1989;1:1429–31.
66. Astrup A, Gotzsche PC, van de WK, Ranneries C, Toubro S, Raben A, *et al*. Meta-analysis of resting metabolic rate in formerly obese subjects. Am J Clin Nutr 1999;69:1117–22.
67. Coxon A, Kreitzman S, Brodie D, Howard A. Rapid weight loss and lean tissue: evidence for comparable body composition and metabolic rate in differing rates of weight loss. Int J Obes 1989;13(Suppl 2):179–81.
68. Weight cycling. National Task Force on the Prevention and Treatment of Obesity. JAMA 1994;272: 1196–202.
69. Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, *et al*. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. Lancet 2001;357: 251–6.