



Published in final edited form as:

*Arthritis Care Res (Hoboken)*. 2022 April ; 74(4): 607–616. doi:10.1002/acr.24765.

## Changes in body weight and knee pain in adults with knee osteoarthritis 3.5 years after completing diet and exercise interventions.:

### The IDEA-follow-up study

Stephen P. Messier, Ph.D.<sup>1,4,10</sup>, Jovita J. Newman, M.S.<sup>2</sup>, Matthew J. Scarlett, M.S.<sup>1</sup>, Shannon L. Mihalko, Ph.D.<sup>2,3</sup>, Gary D. Miller, Ph.D.<sup>2</sup>, Barbara J. Nicklas, Ph.D.<sup>4,2</sup>, Paul DeVita, Ph.D.<sup>5</sup>, David J. Hunter, MBBS, Ph.D.<sup>6</sup>, Mary F. Lyles, M.D.<sup>4</sup>, Felix Eckstein, M.D.<sup>7</sup>, Ali Guermazi, M.D.,Ph.D.<sup>8</sup>, Richard F. Loeser, M.D.<sup>9</sup>, Daniel P. Beavers, Ph.D.<sup>3</sup>

<sup>1</sup>J.B. Snow Biomechanics Laboratory, Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA

<sup>2</sup>Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA

<sup>3</sup>Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA

<sup>4</sup>Section on Gerontology and Geriatric Medicine, Wake Forest School of Medicine

<sup>5</sup>Department of Kinesiology, East Carolina University, Greenville, NC, USA

<sup>6</sup>Rheumatology Department, Royal North Shore Hospital and Institute of Bone and Joint Research, University of Sydney, Sydney, Australia

<sup>7</sup>Department of Imaging & Functional Musculoskeletal Research, Institute of Anatomy & Cell Biology, Paracelsus Medical University, Salzburg & Nuremberg, Salzburg, Austria, & Chondrometrics GmbH, Ainring, Germany & Ludwig Boltzmann Institute for Arthritis and Rehabilitation, Paracelsus Medical University, Salzburg, Austria

<sup>8</sup>Quantitative Imaging Center, Department of Radiology, Boston University School of Medicine, Boston, MA, USA.

<sup>9</sup>Thurston Arthritis Research Center, University of North Carolina School of Medicine, Chapel Hill, NC, USA.

<sup>10</sup>Section on Rheumatology and Immunology, Wake Forest School of Medicine, Winston-Salem, NC, USA

### Abstract

**Objective:** To determine whether long-term diet (D) and exercise (E) interventions, alone or in combination (D+E), have beneficial effects for older adults with knee osteoarthritis 3.5-years after the interventions end.

**Methods:** This is a secondary analysis of a subset (N = 94) of the first 184 participants who had successfully completed the Intensive Diet and Exercise in Arthritis (IDEA) trial (N = 399) and who consented to follow-up testing. Participants were older (age ≥ 55 years), overweight and obese adults with radiographic and symptomatic knee osteoarthritis in at least one knee who completed 1.5-year D+E (N=27), D (N=35), or E (N=32) interventions and returned for 5-year follow-up testing an average of 3.5-years later.

**Results:** During the 3.5-years following the interventions, weight regain in D+E and D was 5.9 kg (7%) and 3.1 kg (4%), respectively, with a 1 kg (1%) weight loss in E. Compared to baseline, weight (D+E, -3.7 kg, P=.0007; D, -5.8 kg, P<.0001; E, -2.9 kg, P=.003) and WOMAC pain (D+E, -1.2, P=.03; D, -1.5, P=.001; E -1.6, P=.0008) were lower in each group at 5-year follow-up. The effect of group assignment at 5-year follow-up was significant for body weight, with D less than E (-3.5 kg, P=.04).

**Discussion—**Older adults with knee osteoarthritis who completed 1.5-year diet or diet plus exercise interventions experienced partial weight regain 3.5 years later, yet relative to baseline, they preserved statistically significant changes in weight loss and reductions in knee pain.

Osteoarthritis (OA) is the most common form of arthritis, the knee is the most often affected weight-bearing joint, and overweight/obesity is a major and modifiable risk factor (1). For three decades the obesity rate has increased such that 70% of the US adult population is either overweight or obese (2), including a similar proportion of adults with arthritis (3). Behavioral interventions targeting diet-induced weight loss and exercise in older adults with knee OA achieve an initial weight loss of at least 5%, resulting in clinically important health benefits (4,5).

The difficulty in losing weight and preventing weight regain in adults was documented in 1959, reinforcing the belief that the path to permanent weight loss has challenging biological (e.g., decrease resting metabolic rate, increase appetite), psychosocial (e.g., decreased self-efficacy, using food for comfort), and environmental (e.g., large food portions, food availability) obstacles (6–8). The difficulty in maintaining weight loss has changed little since those early studies. The National Institutes of Health and the Obesity Society report that weight loss maintenance remains the most challenging aspect of obesity treatment (9). Over 62% of adults with obesity report having lost ≥ 10% of body weight at least once, yet only 20% of overweight adults are successful at maintaining a weight loss of 7–10% for at least one year (7,10). Most individuals who lose weight regain most of their lost weight within five years (11); however, improvements in physical function may be preserved for at least three years (12).

Long-term weight-loss maintenance trials in persons with knee OA are uncommon. One attempt at maintenance of a 10% reduction (8–11 kg) in baseline body weight resulted in a weight regain of less than 2 kg at 3-year follow-up (13). While weight regain was limited, the weight-loss maintenance phase included periods of supervised weight-loss and booster sessions. Without periodic supervision, there is little evidence that long-term weight-loss maintenance in older patients, with and without knee OA, is successful (12).

The Intensive Diet and Exercise for Arthritis (IDEA) trial found a significantly greater reduction in knee pain consequent to a 1.5 year diet and exercise intervention compared to either intervention alone (14). The objectives of this follow-up study were: (1) to document the post-treatment regression or improvement in clinical outcomes 3.5 years after completing diet and exercise interventions, alone or in combination, (2) to quantify the longitudinal changes from baseline to 5-year follow-up, and (3) to determine whether the clinical outcomes at 5-year follow-up were dependent on group assignment.

## MATERIALS AND METHODS

### Study Design

The parent IDEA trial was a single-blind, single-center, 1.5-year, randomized controlled trial conducted at Wake Forest University and Wake Forest School of Medicine between July 2006 and April 2011(14). Randomization of participants (N = 454) was into one of three groups: Diet + Exercise (D+E), Diet (D), or Exercise (E). This follow-up study collected data 5-years (median = 59 months, range, 28 to 64 months) after initial IDEA randomization (FU5), or an average of 3.5 years after completion of the 1.5-year trial (FU1.5) (Figure 1).

Aside from the participants receiving their individual and group results, there was no interaction between participants and study personnel during the 3.5 years between follow-up visits. The Human Subjects Committee of Wake Forest Health Sciences approved the follow-up study. Informed consent was obtained verbally and in writing from all participants between October 2011 and May 2012.

### Study Sample

The pool of potential participants was limited to the first 184 that completed the original IDEA trial due to funding and the availability of research personnel; 94 consented to participate. Participants completed one in-person follow-up visit to the clinic, with a phone interview as an alternate choice. Inclusion criteria for IDEA at baseline included: Kellgren-Lawrence grade 2 or 3 (mild or moderate) radiographic tibiofemoral OA or tibiofemoral plus patellofemoral OA of one or both knees, pain on most days due to knee OA, 27 kg/m<sup>2</sup> body mass index (BMI)  $\geq 41$ kg/m<sup>2</sup>, and a sedentary lifestyle (< 30 minutes per week of structured exercise for the past 6 months). Exclusion criteria included: severe manifestations of coronary heart disease, knee or hip replacement, age < 55 years, receiving knee injections, participating in another ongoing research study, current knee surgery, no knee pain, difficulty with activities of daily living, treatment for cancer other than skin cancer, leaving the area for > 3 months, or consuming 21 or more alcoholic drinks per week.

### Measurements and Procedures

Archival data collected at baseline, and at the end of the IDEA 1.5-year trial (FU1.5), were included with one follow-up visit an average of 5-years from baseline (FU5). Body weight, BMI, waist circumference, the Western Ontario McMasters Universities Osteoarthritis Index (WOMAC) pain and function subscales, 6-minute walk distance, and the Physical Activity Scale for the Elderly (PASE) were collected at FU5 using the same procedures and research technicians blinded to group assignment used in the IDEA trial. Participants also answered

a 24-item health-related questionnaire about current and past tobacco and alcohol use, and current comorbid conditions. Questions regarding health events that occurred since completion of the IDEA trial included surgical procedures such as knee replacements and knee injections, and the number and reasons for hospitalizations. Participants also indicated whether they experienced intentional or unintentional weight loss during the 3.5-year period following completion of the IDEA trial. Pre-specified outcomes not included in this analysis were, 36-Item Short Form Survey (SF-36), and the Short Physical Performance Battery (SPPB).

Body weight (kg), BMI ( $\text{kg}/\text{m}^2$ ), and waist circumference (m) were measured using standard techniques. A 10% larger waist circumference corresponds to a 1.5 times higher mortality over the whole range of waist circumferences (15). The WOMAC pain subscale (16) measures self-reported pain on a scale from 0 (none) to 4 (extreme) the degree of pain experienced performing daily living activities in the last 48 hours due to knee OA. Total scores for the 5 items range from 0–20; higher scores indicate greater pain. Participants that had undergone unilateral total knee replacement surgery during follow-up recorded the pain in their non-surgical knee. The WOMAC self-reported function subscale includes 17 items that are added to generate a summary score ranging from 0 to 68; higher scores indicate poorer function. The relative minimally clinically important improvement from baseline for pain and function  $[(\text{final} - \text{baseline})/\text{baseline}]$  is 20% (17). Six-minute walk distance (m) was our measure of clinical mobility. Changes exceeding 30.5 m are considered clinically meaningful (18). The PASE scale was used to estimate activity levels with higher scores (range 0–400) indicating greater activity (19).

### Statistical Analysis

These analyses utilized the complete IDEA trial dataset (baseline,  $N = 454$ ; 18 months,  $N = 399$ ) that included the 94, 5-year follow-up participants that were recruited from a pool of 184 participants that were the first to complete the trial. Hence, all primary comparisons are adjusted based on the main trial characteristics, making the findings less likely to be affected by nonrandom processes contributing to long-term study nonparticipation. To determine if the sample at 5-year follow-up was representative of the potential pool of the first 184 randomized IDEA participants, and of the entire IDEA cohort ( $N = 454$ ), independent t-tests and  $\chi^2$  tests identified the differences among continuous and categorical baseline characteristics. The effects of the interventions on patient reported outcomes were determined using mixed model regression analyses with main effects of treatment assignment, visit, and treatment by visit interaction, adjusted for IDEA randomization stratification factors (sex and baseline BMI) and baseline estimates of outcomes when available. Statistical analyses included all follow-up data from baseline measurements, and visit specific estimates were determined using contrast statements. The intervention effects were reported using mean estimates with standard errors and 95% confidence intervals (95% CI) at each follow-up visit. Within-group changes from baseline to FU5, and from FU1.5 to FU5 were reported using mean estimates and 95% CIs. Pairwise comparisons assessed the differences between groups at the FU5 visit. Post treatment assessment also included the number of participants in each group that achieved 5% or 10% weight loss at completion of the 1.5-year interventions and at 5-year follow-up. A sensitivity analysis

of the effect on outcome measures of total knee replacement during the 3.5-year follow-up period was examined using analysis of co-variance with and without adjusting for total knee replacement.

Additional sensitivity analyses used multiple imputation to assess between group treatment effects accounting for potential bias due to missing data for all 454 randomized individuals in the IDEA study. All statistical analyses were performed using SAS version 9.4 with a Type 1 error rate of .05 for overall treatment and pairwise comparisons. Unadjusted within-group comparisons of body weight and WOMAC pain at baseline, and 1.5- and 5-year follow-ups are presented using box and whisker plots.

## RESULTS

Of the first 184 IDEA participants that successfully completed 1.5-year testing, 94 (51%) consented to follow-up testing 3.5-years later or approximately 5-years from baseline (median, 59 months; range, 27 to 64 months). The 90 participants that did not attend a 5-year follow-up session were similar to the 94 participants that attended, with the exception of age (did not attend FU5, 65.1 (6.1) yrs., attended FU5, 67.4 (6.1) yrs.,  $P = .002$ , Table 1). Distribution, N (% female), was D+E, 27 (78); D, 35 (63); and E, 32 (66). Baseline body weight (D+E, 93.0 kg, D, 93.4 kg, E, 92.3 kg) and BMI (D+E, 33.6 kg/m<sup>2</sup>, D, 33.7 kg/m<sup>2</sup>, E, 33.5 kg/m<sup>2</sup>) were not statistically different between the groups (Table 1). Thirteen participants completed the 5-year follow-up visit via the phone with trained study personnel; all others (N = 81) agreed to in-person testing at the clinic. With the exception of age, the sample of 94 IDEA follow-up participants was also representative of all 360 participants enrolled in the IDEA trial that did not undergo testing at 5-year follow-up (Table 1).

### Post-treatment regression/improvement

During the 3.5-years following the interventions, 34 participants had at least one knee injection, 10 (38%) in D+E, 15 (43%) in D, and 8 (25%) in E,  $P = .29$ . In addition, 11 participants had unilateral total knee replacements and three (2 in D+E and 1 in E) had bilateral replacements, a total of 17 total knee replacements; D+E, 4, D, 8, and E, 5,  $P = .65$ . Other knee joint surgeries were D+E, 2 (7%), D, 3 (9%), and E, 4 (13%),  $P = .56$ . Table 2 includes additional co-morbid conditions that occurred during the follow-up period. Intentional weight-loss attempts initiated during the follow-up period were common in all groups (53/89, 5 did not answer), D+E, 14, D, 19, and E, 20. Weight loss that occurred due to illness (4/94) was D+E, 1, D, 2, and E 1.

Body weight increased during the 3.5-year follow-up period in D+E by 5.9 kg (7%), ( $P < .0001$ ), and in D by 3.1 kg (4%), ( $P = .0006$ ), but decreased in E by -1.0 kg (1%), ( $P = .25$ ). Ninety-one percent of the D+E group and 80% of the D group achieved a 5% weight loss at 1.5 years; 57% and 68% respectively maintained a 5% weight-loss at 5-year follow-up. A 10% weight loss was achieved by 71% of the D+E group and 52% of the D group at 1.5 years; 19% and 36% respectively maintained a 10% weight-loss at 5-year follow-up. The E group increased the number of participants that achieved a 5% weight loss from 18% at 1.5 years to 29% at 5-year follow-up; a 10% weight loss was achieved by 7% of the E group at 1.5 and 5-year follow-up (Table 3). BMI increased in D+E, (difference, 2.2 kg/m<sup>2</sup>,

$P < .0001$ ) and D, (difference,  $1.1 \text{ kg/m}^2$   $P = .0004$ ), but decreased in E, (difference,  $-0.4 \text{ kg/m}^2$ ,  $P = .20$ ). Waist circumference increased in D+E, (difference,  $8.4 \text{ cm}$ ,  $P < .0001$ ), D, (difference,  $1.0 \text{ cm}$ ,  $P = .39$ ), and in E, (difference,  $1.3 \text{ cm}$ ,  $P = .24$ ) (Table 4).

WOMAC pain worsened significantly in D+E (difference,  $1.9$ ,  $P = .0003$ ), and remained unchanged in D (difference,  $0.0$ ,  $P = .96$ ) and in E (difference,  $0.2$ ,  $P = .62$ ). WOMAC function declined significantly in D+E (difference,  $4.4$ ,  $P = .005$ ), but remained unchanged in D (difference,  $0.7$ ,  $P = .62$ ) and in E (difference,  $0.9$ ,  $P = .55$ ). There was a significant reduction in 6-minute walk distance across all groups between the end of the 1.5 year intervention and 5-year follow-up: D+E,  $-99 \text{ m}$  ( $P < .0001$ ), D,  $-57 \text{ m}$  ( $P < .0001$ ), and E,  $-64 \text{ m}$  ( $P < .0001$ ). Physical activity levels regressed during the 3.5 years following the intervention in D (difference,  $-26$ ,  $P = .053$ ) and in E (difference,  $-26$ ,  $P = .004$ ), but remained closer to FU1.5 levels in D+E (difference,  $-13$ ,  $P = .19$ ) (Table 4).

### Longitudinal changes from baseline to 5-year follow-up

From baseline to 5-year follow-up, all groups significantly reduced body weight. Mean weight-loss was  $-3.7 \text{ kg}$  for the D+E group ( $P = .0007$ ),  $-5.8 \text{ kg}$  for the D group ( $P < .0001$ ), and  $-2.9 \text{ kg}$  for the E group ( $P = .003$ ). Changes in BMI were D+E,  $-1.2 \text{ kg/m}^2$  ( $P = .001$ ), D,  $-2.0 \text{ kg/m}^2$  ( $P < .0001$ ) and E,  $-1.0 \text{ kg/m}^2$  ( $P = .004$ ). The D group significantly reduced waist circumference by  $-6.2 \text{ cm}$  ( $P < .0001$ ); however, the  $0.4 \text{ cm}$  increase in the D+E ( $P = .73$ ) group and  $0.0 \text{ cm}$  change ( $P = .98$ ) in the E groups were not significantly different from baseline. Figure 2a shows the unadjusted body weight changes by group.

Each group significantly attenuated WOMAC pain across the 5-year follow-up period. Reductions in pain were D+E,  $-1.2$ , ( $P = .03$ ), D,  $-1.5$  ( $P = .001$ ), and E,  $-1.6$  ( $P = .0008$ ). Figure 2b shows similar patterns of change in the unadjusted data. WOMAC function significantly improved in each group relative to baseline values: D+E,  $-6.2$  ( $P = .0001$ ), D,  $-6.1$  ( $P < .0001$ ), and E,  $-3.7$  ( $P = .01$ ). At 5-year follow-up, 6-min walk distance was significantly shorter compared to baseline in D+E,  $-26 \text{ m}$  ( $P = .02$ ) and in D,  $-38 \text{ m}$  ( $P = .0002$ ), but not in E,  $-16 \text{ m}$  ( $P = .10$ ). Changes in physical activity levels were similar to baseline across all groups (D+E,  $13$ ,  $P = .19$ ; D,  $0$ ,  $P = .98$ ; E,  $5$ ,  $P = .58$ )

### Effects of group assignment

At 5-years, there was no significant difference in body weight between D+E and D,  $89.5 \text{ kg}$  vs  $87.6 \text{ kg}$  ( $P = .18$ ), or E,  $89.5 \text{ kg}$  vs  $90.1 \text{ kg}$  ( $P = .26$ ), but D was less than E,  $87.6 \text{ kg}$  vs  $90.1 \text{ kg}$  ( $P = .04$ ). Similar results occurred for BMI; D+E vs D,  $32.5 \text{ kg/m}^2$  vs  $31.8 \text{ kg/m}^2$  ( $P = .21$ ), D+E vs E,  $32.5 \text{ kg/m}^2$  vs  $32.6 \text{ kg/m}^2$  ( $P = .25$ ), and D vs E,  $31.8 \text{ kg/m}^2$  vs  $32.6 \text{ kg/m}^2$  ( $P = .05$ ). Waist circumference was not statistically different between the groups, D+E vs D,  $107.0 \text{ cm}$  vs  $101.1 \text{ cm}$  ( $P = .09$ ), D+E vs E,  $107.0 \text{ cm}$  vs  $106.4 \text{ cm}$  ( $P = .90$ ), and for D vs E,  $101.1 \text{ cm}$  vs  $106.4 \text{ cm}$  ( $P = .11$ ) (Table 4). All groups remained classified as class I obese at 5-year follow-up.

Pairwise comparisons at 5-year follow-up revealed no significant difference in WOMAC pain in D+E compared to D,  $5.4$  vs  $4.8$  ( $P = .68$ ), and E,  $5.4$  vs  $5.0$  ( $P = .65$ ), and in D compared to E,  $4.8$  vs  $5.0$  ( $P = .90$ ). WOMAC function (D+E vs D,  $17.9$  vs  $17.9$ ,  $P = .78$ , D+E vs E,  $17.9$  vs  $19.4$ ,  $P = .58$ , D vs E,  $17.9$  vs  $19.4$ ,  $P = .83$ ), and 6-minute walk distance



(D+E vs D, 456 m vs 447 m,  $P = .70$ , D+E vs E, 456 m vs 465 m,  $P = .81$ , D vs E, 447 m vs 465 m,  $P = .37$ ) were not significantly different between groups. There was no significant difference between the groups at 5-year follow-up in PASE physical activity levels (D+E vs D, 130 vs 116,  $P = .29$ , D+E vs E, 130 vs 118,  $P = .25$ , D vs E, 116 vs 118,  $P = .99$ ) (Table 4).

A comparison of outcomes at 5-year follow-up with and without adjustment for total knee replacement ( $N = 17$ ) showed similar values within each measurement and between groups (Supplement eTable 1).

## DISCUSSION

Among participants with knee osteoarthritis that completed 1.5-year diet and exercise interventions, alone or in combination, each group experienced statistically significant reductions in body weight, BMI, pain, and improvement in function relative to baseline values 3.5-years after completing the interventions. At 5-year follow-up the D group maintained significantly lower body weight and BMI compared to the E group.

The minimally clinically important improvement in pain and function established by OMERACT-OARSI is 20% from baseline (17). Five years after baseline testing, participants randomized to the D group maintained 27% (1.5 units) and 28% (6.1 units) mean improvements in pain and function, respectively. However, the 95% CI around pain improvement included worse scores near zero, suggesting no clinical benefit remained for some participants. The D group also maintained a 5.8 kg (6%) mean weight loss that resulted in a 2 kg/m<sup>2</sup> reduction in BMI from baseline, along with a waist circumference that was 6 cm smaller. Comparable improvements were also present in the D+E and E groups. Taken together, these results suggest that completing 1.5-year diet and/or exercise interventions in older adults with knee osteoarthritis result in statistically significant and clinically important improvements in clinical outcomes 5-years from baseline.

Without an active intervention, older patients (age  $\geq 65$  years) with knee pain experience statistically significant declines in strength, balance, and mobility, and an increase in disability (20,21). Further, the odds of OA progression increase in people who gain weight compared to those that maintain weight later in life (22). Weight loss via diet and/or exercise in randomized clinical trials is generally less than 10%, and weight-loss maintenance years after an obesity treatment ends is poor (8). More encouraging, however, are that long-term changes similar to the D group (6% weight loss, 1.5 unit reduction in pain), and to a lesser extent the D+E (4% weight loss, 1.2 unit reduction in pain) and E (3% weight loss and 1.6 unit reduction in pain) groups, could be important public health outcomes for older, overweight and obese adults with knee OA.

We posited the reason for the significant improvements in most clinical outcomes in D+E relative to D and E during the IDEA trial was the psycho-physiological effect of exercise on the nervous system, that when combined with weight loss, resulted in greater pain reduction and improvement in many clinical outcomes (14). Three-plus years after completing the IDEA interventions, however, the D+E group experienced greater regression toward baseline

values than the D and E groups; the D+E group regained 5.8 kg in body weight coupled with an 8.4 cm mean increase in waist circumference. Fewer D+E participants maintained a 5% or 10% weight loss at 5 years compared to the D group. Prior studies observed that weight regain in older adults was primarily fat mass, with less regain of muscle mass. Hence, the worsening of body composition may also be a factor in the intensification of pain in those with prior weight loss (23–25). The interaction of weight regain with the absence of regular exercise in the D+E group may have exacerbated the regression in clinical outcomes compared to either intervention alone.

The E group was the only group to record a mean weight loss during the 3.5-years following completion of the intervention (−0.9 kg), resulting in an overall 2.2 kg weight loss from baseline. PASE physical activity levels regressed to near baseline values and mobility, represented by 6-minute walk distance, was below the mean baseline value. Yet, pain remained virtually unchanged from the end of the exercise intervention, and 18% less than at baseline. Exercise has a consistent but modest effect on clinical outcomes in knee OA patients (26), and these improvements are maintained 3.5 years after the intervention has ended.

This study had several limitations. Of the 184 participants contacted, only 51% (94) participated in this follow-up study. However, tests for equivalence at baseline determined that individuals who did return were representative of the pool of 184 potential participants, and of the entire IDEA cohort, including loss to follow-up participants. Also, multiple imputation was used due to the potential bias of missing data. Thirteen participants opted to complete the 5-year follow-up visit via the phone; hence, waist circumference and 6-minute walk were missing data. Furthermore, these 13 participants provided self-reported body weight, which increased the chance of response bias. Finally, 14 participants had 17 total knee replacement surgeries during the 3.5-year follow-up. Analysis of 5-year outcomes with and without adjusting for total knee replacements yielded similar results (Supplement eTable 1).

## CONCLUSION

The normal trajectory for community-dwelling older adults with knee osteoarthritis is one of weight gain and a consistent knee pain profile (27,28). In contrast, older adults with knee osteoarthritis who completed 1.5-year diet or diet plus exercise interventions experienced partial weight regain, but preserved statistically significant changes in weight loss and reductions in knee pain relative to baseline 5-years after study randomization. The exercise group experienced no weight regain and had similar improvements in pain to the two diet groups. These data imply that clinicians who treat people with knee osteoarthritis have a variety of non-pharmacologic options that preserve clinically important effects 3.5 years after the treatments end.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.



## Funding/Support:

Support for this study was provided by grants from the National Institutes of Health: R01 AR052528-01 from NIAMS, P30 AG21332 from NIA, M01-RR00211 from NCRR, and General Nutrition Centers, Inc.

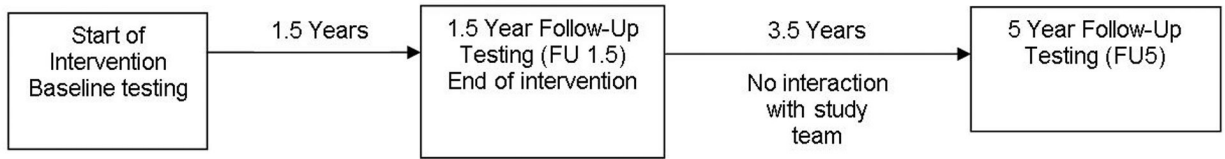
## References

1. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society*. 2010 Jan;18(1):24–33.
2. Prevention C for DC and. Health, United States, 2016 [Internet]. National Center for Health Statistics; 2016 p. 237–41. Available from: <https://www.cdc.gov/nchs/hus/index.htm>
3. Guglielmo D Hootman JM, Murphy LB, Boring MA, Theis KA, Belay B, Barbour KE, Cisternas MG, Helmick CG. Health care provider counseling for weight loss among adults with arthritis and overweight or obesity- United States, 2002–2014. Vol. 67, prevention, Centers for disease control and. 2018. p. 487–91.
4. Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum*. 2004 May;50(5):1501–10. [PubMed: 15146420]
5. Messier SP, Resnik AE, Beavers DP, Mihalko SL, Miller GD, Nicklas BJ, et al. Intentional Weight Loss for Overweight and Obese Knee Osteoarthritis Patients: Is More Better? *Arthritis Care Res (Hoboken)*. 2018 Jun 18;
6. Stunkard A, Mc L-HM. The results of treatment for obesity: a review of the literature and report of a series. *AMA archives of internal medicine*. 1959 Jan;103(1):79–85. [PubMed: 13605305]
7. Wing RR, Phelan S. Long-term weight loss maintenance. *AmJClinNutr*. 2005 Jul;82(1 Suppl):222S–225S.
8. Brownell KD. The humbling experience of treating obesity: Should we persist or desist? *BehavResTher*. 2010 Aug;48(8):717–9.
9. MacLean PS, Wing RR, Davidson T, Epstein L, Goodpaster B, Hall KD, et al. NIH Working Group Report: Innovative Research to Improve Maintenance of Weight Loss. *Obesity (Silver Spring)*. 2015 Jan;23(1):7–15. [PubMed: 25469998]
10. McGuire MT, Wing RR, Hill JO. The prevalence of weight loss maintenance among American adults. *Int J Obes Relat Metab Disord*. 1999 Dec;23(12):1314–9. [PubMed: 10643690]
11. Methods for voluntary weight loss and control. NIH Technology Assessment Conference Panel. Consensus Development Conference, 30 March to 1 April 1992. *Ann Intern Med*. 1993 Oct 1;119(7 Pt 2):764–70. [PubMed: 8363212]
12. Houston DK, Miller ME, Kitzman DW, Rejeski WJ, Messier SP, Lyles MF, et al. Long-Term Effects of Randomization to a Weight Loss Intervention in Older Adults: A Pilot Study. *J Nutr Gerontol Geriatr*. 2019 Mar 8;1–17.
13. Christensen P, Henriksen M, Bartels EM, Leeds AR, Meinert Larsen T, Gudbergesen H, et al. Long-term weight-loss maintenance in obese patients with knee osteoarthritis: a randomized trial. *The American journal of clinical nutrition*. 2017 Sep;106(3):755–63. [PubMed: 28747328]
14. Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, Devita P, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA*. 2013 Sep 25;310(12):1263–73. [PubMed: 24065013]
15. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol*. 2020;16(3):177–89. [PubMed: 32020062]
16. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt L. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes following total hip or knee arthroplasty in osteoarthritis. *Journal of Orthopaedic Rheumatology*. 1988;1:95–108.

17. Tubach F, Ravaud P, Martin-Mola E, Awada H, Bellamy N, Bombardier C, et al. Minimum clinically important improvement and patient acceptable symptom state in pain and function in rheumatoid arthritis, ankylosing spondylitis, chronic back pain, hand osteoarthritis, and hip and knee osteoarthritis: Results from a prospective multinational study. *Arthritis Care Res(Hoboken)*. 2012 Nov;64(11):1699–707. [PubMed: 22674853]
18. Bohannon RW, Crouch R. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *J Eval Clin Pract*. 2017 Apr;23(2):377–81. [PubMed: 27592691]
19. Washburn RA, McAuley E, Katula J, Mihalko SL, Boileau RA. The physical activity scale for the elderly (PASE): evidence for validity. *J Clin Epidemiol*. 1999 Jul;52(7):643–51.
20. Miller ME, Rejeski WJ, Messier SP, Loeser RF. Modifiers of change in physical functioning in older adults with knee pain: the Observational Arthritis Study in Seniors (OASIS). *Arthritis Rheum*. 2001 Aug;45(4):331–9. [PubMed: 11501720]
21. Messier SP, Glasser JL, Ettinger WH, Craven TE, Miller ME. Declines in strength and balance in older adults with chronic knee pain: A 30-month longitudinal, observational study. *Arthritis & Rheumatism-Arthritis Care & Research*. 2002 Apr 15;47(2):141–8. [PubMed: 11954007]
22. Bucknor MD Nardo L, Joseph GB, Alizai H, Srikkum W, Nevitt MC, Lynch JA, McCulloch CE, Link TM. Association of cartilage degeneration with four year weight gain-3T MRI data from the Osteoarthritis Initiative. 2015.
23. Beavers KM, Lyles MF, Davis CC, Wang X, Beavers DP, Nicklas BJ. Is lost lean mass from intentional weight loss recovered during weight regain in postmenopausal women? *Am J Clin Nutr*. 2011 Sep;94(3):767–74. [PubMed: 21795437]
24. Beavers KM, Neiberg RH, Houston DK, Bray GA, Hill JO, Jakicic JM, et al. Body weight dynamics following intentional weight loss and physical performance: the Look AHEAD Movement and Memory Study: Weight fluctuation and physical performance. *Obesity Science & Practice*. 2015 Oct;1(1):12–22. [PubMed: 27453790]
25. Chmelo EA, Beavers DP, Lyles MF, Marsh AP, Nicklas BJ, Beavers KM. Legacy effects of short-term intentional weight loss on total body and thigh composition in overweight and obese older adults. *Nutrition & diabetes*. 2016 Apr 4;6:e203. [PubMed: 27043417]
26. Bennell KL, Hinman RS. A review of the clinical evidence for exercise in osteoarthritis of the hip and knee. *Journal of science and medicine in sport*. 2011 Jan;14(1):4–9. [PubMed: 20851051]
27. Gademan MGJ, Putter H, Van Den Hout WB, Kloppenburg M, Hofstede SN, Cannegieter SC, et al. The course of pain and function in osteoarthritis and timing of arthroplasty: the CHECK cohort. *Acta Orthop*. 2018 Oct;89(5):528–34. [PubMed: 30350757]
28. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med*. 1988 Jul 1;109(1):18–24.

### SIGNIFICANCE AND INNOVATIONS

- The normal trajectory for community-dwelling older adults with knee osteoarthritis is one of weight gain and a consistent knee pain profile. In contrast, older adults with knee osteoarthritis who completed 1.5-year diet or diet plus exercise interventions experienced partial weight regain 3.5 years later, yet relative to baseline, they preserved statistically significant changes in weight loss and reductions in knee pain.
- Taken together, these results suggest that diet and/or exercise interventions are effective non-pharmacologic treatments for older adults with knee osteoarthritis that can result in improved clinical outcomes more than 3 years after the treatments end.
- These data imply that clinicians who treat people with knee osteoarthritis have a variety of non-pharmacologic options that preserve clinically important effects.



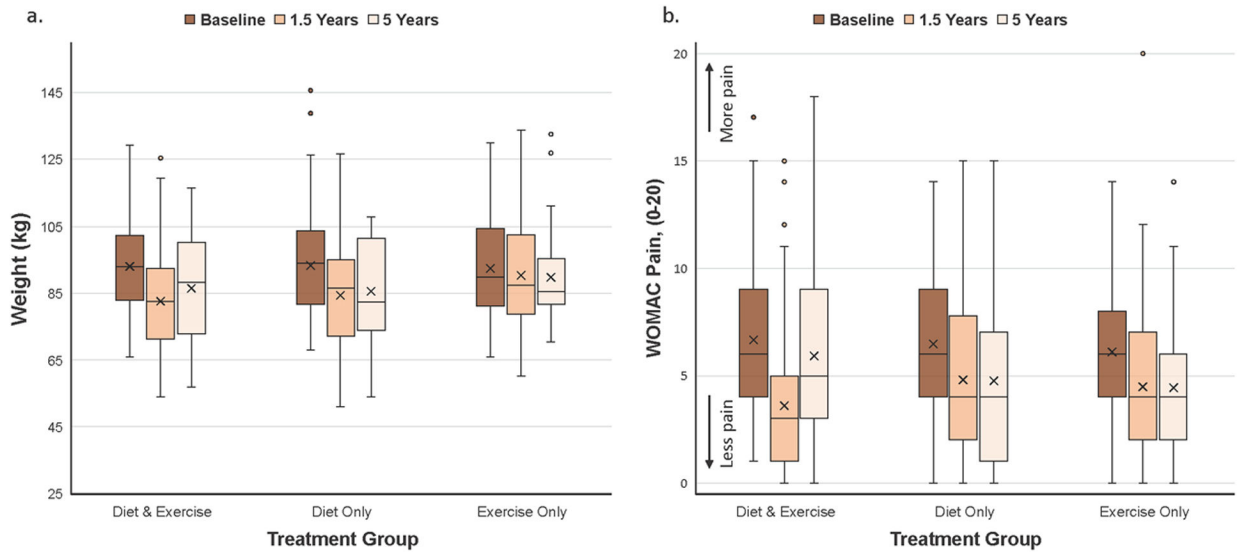
**Figure 1.** The timeline of the IDEA randomized clinical trial of diet and exercise with follow-up testing.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript



**Figure 2.**

a. Unadjusted body weight and b. WOMAC pain scores from baseline to the end of the interventions at 1.5 year follow-up, and to 5-year follow-up for the diet and exercise (D+E), diet (D), and exercise (E) groups.

The middle line in the plot boxes represent the median values; the X, the mean values; and the boxes, the interquartile range. The whiskers extend to the most extreme observed values within 1.5 x the interquartile range of the nearer quartile, and the dots represent observed values outside the range.

**Table 1.**

Comparison of baseline characteristics of the participants that returned for 5-year follow-up testing (N = 94) to those that did not return for 5-year testing (either unwilling or could not be contacted, N = 90), and to all participants that were not included in 5-year follow-up (FU) testing (N = 360).

Variable	Returned for 5-year FU testing	Did not return for 5-year FU testing (unwilling or could not be contacted)	P-value (returned vs. did not return)	All participants not included in 5-year FU testing	P-value (returned vs. all participants not included)
N	94	90		360	
Sex, No. Females (%)	64 (67)	66 (73)	.44	261 (73)	.31
Race, No. White (%)	84 (88)	74 (82)	.24	293 (82)	.12
Age, years	67.4 (6.1)	65.0 (5.6)	.006	65.1 (6.1)	.002
Height, cm	166.2 (9.7)	164.7 (8.8)	.29	166.0 (9.0)	.82
Body weight, kg	91.7 (14.4)	91.9 (13.8)	.93	93.2 (14.8)	.36
BMI, kg/m <sup>2</sup>	33.1 (3.3)	33.8 (3.6)	.17	33.7 (3.8)	.11
Waist circumference cm	106.4 (11.7)	106.7 (11.3)	.80	106.7 (12.0)	.81
6-min walk distance m	484.6 (76.9)	471.1(87.6)	.28	470.9 (89.0)	.17
Walk speed, m/s	1.20 (0.19)	1.17 (0.20)	.39	1.21 (0.18)	.60
WOMAC pain (0 none - 20 extreme)	6.4 (2.9)	6.8 (2.9)	.37	6.5 (3.2)	.82
WOMAC function (0 best - 68 worst)	24.2 (10.7)	26.3 (10.6)	.19	24.2 (10.9)	.95
PASE (0 low - 400 high)	116 (57)	107 (48)	.25	114 (51)	.71



**Table 2.**

Frequency N (%) of the onset of significant health events during the 3.5-years following the completion of the diet and exercise interventions.

<b>Co-morbid condition</b>	<b>Diet + Exercise</b>	<b>Diet</b>	<b>Exercise</b>	<b>P value</b>
<b>Knee Injections</b>	10 (38)	15 (43)	8 (25)	.29
<b>Knee Replacements</b>	4 (15)	8 (23)	5 (16)	.67
<b>Other knee surgeries</b>	2 (7)	3 (9)	4 (13)	.80
<b>Type II Diabetes</b>	4 (15)	3 (9)	8 (25)	.19
<b>Coronary Artery Disease</b>	3 (13)	2 (6)	4 (13)	.61
<b>Stroke/Transient Ischemic Attack</b>	1 (4)	2 (6)	4 (13)	.45

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

**Table 3.**

The number and percentage of participants in the Diet + Exercise, Diet, and Exercise groups that achieved 5% or 10% weight loss at the end of the 1.5-year intervention and at 5-year follow-up.

Intervention Group	N <sup>b</sup>	5% Weight Loss <sup>a</sup>		10% Weight Loss	
		1.5 year FU <sup>c</sup> No. (%)	5-year FU No. (%)	1.5 year FU No. (%)	5-year FU No. (%)
Diet+Exercise	21	19 (91)	12 (57)	15 (71)	4 (19)
Diet	25	20 (80)	17 (68)	13 (52)	9 (36)
Exercise	28	5 (18)	8 (29)	2 (7)	2 (7)

<sup>a</sup>The 5% weight loss group includes participants in the 10% weight loss group.

<sup>b</sup>The number of participants (N) in each group includes those with documented weights at both 1.5 and 5-year follow-ups.

<sup>c</sup>FU = follow-up

**Table 4.**

Between group differences and within group changes in anthropometric, clinical, and functional outcomes for the diet and exercise, diet, and exercise groups at baseline, 1.5-year follow-up (FU1.5), and 5-year follow-up (FU5).

	Diet + Exercise	P	Diet	P	Exercise	P	Mean Difference (95% CI) at FU5	P
<b>Body weight (kg)</b>								
IDEA Baseline (95% CI)	93.0 (90.7, 95.3)		93.4 (90.9, 95.9)		92.3 (88.6, 95.9)			
1.5-year follow-up (95% CI)	83.7 (82.4, 84.9)		84.5 (83.3, 85.8)		91.0 (89.8, 92.3)			
5-year follow-up (95% CI)	89.5 (87.6, 91.4)		87.6 (85.5, 89.8)		90.1 (88.0, 92.1)			.07 <sup>a</sup>
Diet + Exercise vs Diet <sup>b</sup>							2.0 (-1.0, 4.9)	.18
Diet + Exercise vs Exercise							-1.6 (-4.3, 1.2)	.26
Diet vs Exercise							-3.5 (-6.9, -0.2)	.04
<b>Within Group Change (95% CI)</b>								
FU5 - FU1.5	5.9 (3.9, 7.8)	<.0001	3.1 (1.3, 4.9)	.0006	-1.0 (-2.7, 0.7)	.25		
FU5 - Baseline	-3.7 (-5.9, -1.6)	.0007	-5.8 (-7.8, -3.8)	<.0001	-2.9 (-4.8, -1.0)	.003		
<b>BMI (kg/m<sup>2</sup>)</b>								
IDEA Baseline (95% CI)	33.6 (33.0,34.2)		33.7 (33.1,34.3)		33.5 (32.9,34.1)			
1.5-year follow-up (95% CI)	30.3 (29.9,30.7)		30.7 (30.3,31.1)		33.0 (32.6,33.4)			
5-year follow-up (95% CI)	32.5 (31.7,33.2)		31.8 (31.1,32.5)		32.6 (31.9,33.2)			.08
Diet + Exercise vs Diet							0.7 (-0.4, 1.7)	.21
Diet + Exercise vs Exercise							-0.6 (-1.6, 0.4)	.25
Diet vs Exercise							-1.3 (-2.5, -0.0)	.05
<b>Within Group Change (95% CI)</b>								
FU5 - FU1.5	2.2 (1.5, 2.8)	<.0001	1.1 (0.5, 1.7)	.0004	-0.4 (-1.0, 0.2)	.20		
FU5 - Baseline	-1.2 (-1.9, -0.5)	.001	-2.0 (-2.7, -1.3)	<.0001	-1.0 (-1.6, -0.3)	.004		
<b>Waist Circumference (cm)</b>								
IDEA Baseline (95% CI)	106.2 (104.3,108.1)		107.1 (105.1,109.1)		106.6 (105.3,107.9)			
1.5-year follow-up (95% CI)	98.6 (97.4,99.9)		100.1 (98.8,101.5)		105.1 (103.7,106.4)			

	Diet + Exercise	P	Diet	P	Exercise	P	Mean Difference (95% CI) at FU5	P
5-year follow-up (95% CI)	107.0 (104.5,109.5)		101.1 (98.8,103.4)		106.4 (104.1,108.7)			.16
Diet + Exercise vs Diet							5.2 (-0.8, 11.2)	.09
Diet + Exercise vs Exercise							0.4 (-5.9, 6.7)	.90
Diet vs Exercise							-4.8 (-10.8, 1.2)	.11
Within Group Change (95% CI)								
FU5 - FU1.5	8.4 (6.0, 10.8)	<.0001	1.0 (-1.3, 3.2)	.39	1.3 (-0.9, 3.6)	.24		
FU5 - Baseline	0.4 (-2.1, 3.0)	.73	-6.2 (-8.5, -3.8)	<.0001	-0.0 (-2.4, 2.3)	.98		
<b>WOMAC Pain (0-20)</b>								
IDEA Baseline (95% CI)	6.7 (6.1,7.2)		6.6 (6.1,7.1)		6.1 (5.6,6.6)			
1.5-year follow-up (95% CI)	3.5 (2.9,4.0)		4.8 (4.3,5.3)		4.7 (4.2,5.3)			
5-year follow-up (95% CI)	5.4 (4.4,6.4)		4.8 (3.9,5.7)		5.0 (4.0,5.9)			.86 <sup>a</sup>
Diet + Exercise vs Diet <sup>b</sup>							0.4 (-1.4, 2.2)	.68
Diet + Exercise vs Exercise							0.5 (-1.7, 2.6)	.65
Diet vs Exercise							0.1 (-1.7, 1.9)	.90
Within Group Change (95% CI)								
FU5 - FU1.5	1.9 (0.9, 2.9)	.0003	0.0 (-0.9, 0.9)	.96	0.2 (-0.7, 1.2)	.62		
FU5 - Baseline	-1.2 (-2.2, -0.1)	.03	-1.5 (-2.4, -0.6)	.001	-1.6 (-2.6, -0.7)	.0008		
<b>WOMAC Function (0-68)</b>								
IDEA Baseline (95% CI)	24.6 (22.7,26.5)		24.8 (23.2,26.5)		23.1 (21.5,24.8)			
1.5-year follow-up (95% CI)	13.5 (11.8,15.1)		17.2 (15.6,18.9)		18.6 (16.9,20.2)			
5-year follow-up (95% CI)	17.9 (14.8,21.0)		17.9 (15.2,20.7)		19.4 (16.6,22.3)			.88
Diet + Exercise vs Diet							-0.8 (-6.3, 4.8)	.78
Diet + Exercise vs Exercise							-1.5 (-6.9, 3.9)	.58
Diet vs Exercise							-0.7 (-7.7, 6.2)	.83
Within Group Change (95% CI)								
FU5 - FU1.5	4.4 (1.3, 7.4)	.005	0.7 (-2.0, 3.4)	.62	0.9 (-2.0, 3.7)	.55		
FU5 - Baseline	-6.2 (-9.4, -3.1)	.0001	-6.1 (-8.9, -3.3)	<.0001	-3.7 (-6.6, -0.8)	.01		

	Diet + Exercise	P	Diet	P	Exercise	P	Mean Difference (95% CI) at FU5	P
<b>6-minute walk distance (m)</b>								
IDEA Baseline (95% CI)	467 (453,480)		475 (462,488)		480 (465,494)			
1.5-year follow-up (95% CI)	555 (543,566)		504 (493,516)		529 (517,540)			
5-year follow-up (95% CI)	456 (435,477)		447 (426,468)		465 (445,484)			.78
Diet + Exercise vs Diet							10.9 (-46.2, 68.0)	.70
Diet + Exercise vs Exercise							-6.8 (-65.1, 51.5)	.81
Diet vs Exercise							-17.7 (-57.0, 21.6)	.37
Within Group Change (95% CI)								
FU5 - FU1.5	-99 (-119, -79)	<.0001	-57 (-77, -38)	<.0001	-64 (-83, -46)	<.0001		
FU5 - Baseline	-26 (-47, -5)	.02	-38 (-59, -18)	.0002	-16 (-35, 3)	.10		
<b>PASE (0-400)</b>								
IDEA Baseline (95% CI)	117 (107,126)		115 (107,124)		111 (103,119)			
1.5-year follow-up (95% CI)	144 (132,151)		133 (123,142)		144 (134, 154)			
5-year follow-up (95% CI)	130 (109,151)		116 (98,134)		118 (99,137)			.48 <sup>a</sup>
Diet + Exercise vs Diet <sup>b</sup>							14 (-13, 41)	.29
Diet + Exercise vs Exercise							15 (-11, 39)	.25
Diet vs Exercise							0 (-31, 30)	.99
Within Group Change (95% CI)								
FU5 - FU1.5	-13 (-32, 6)	.19	-17 (-34, 0)	.053	-26 (-44, -8)	.004		
FU5 - Baseline	13 (-6, 31)	.19	0 (-16, 17)	.98	5 (-12, 22)	.58		

<sup>a</sup>Omnibus p value that represents the overall test for significance among the three 5-year adjusted means. Models were adjusted for sex, baseline BMI, and baseline outcome values.

<sup>b</sup>Intervention effects at FU5 using adjusted pairwise differences and multiple imputation