

Supplemental Online Content

Messier SP, Beavers DP, Queen K, et al. Effect of diet and exercise on knee pain in patients with osteoarthritis and overweight or obesity: a randomized clinical trial. *JAMA*. Published December 13, 2022. doi:10.1001/jama.2022.21893

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Demographic and Clinical Characteristics of the Study Participants at Baseline Using Completers Only.

Baseline Characteristics	Diet + Exercise	Control
No.	377	343
Age, mean (SD), y	64.9 (7.7)	65.1 (7.7)
Weight, mean (SD), kg	99.6 (19.3)	100.8 (22.2)
Height, mean (SD), ft	5.4 ± .3	5.5 ±.3
BMI, mean (SD), kg/m ²	36.4 (6.1)	36.7 (7.2)
Sex, No. (%)		
Women	290 (76.9)	262 (76.4)
Men	87 (23.1)	81 (23.6)
Race, No. (%) ^a		
White	268 (71.1)	231 (67.3)
Black	96 (25.5)	103 (30.0)
Annual household income, No. (%) ^b		
<\$20 000	47 (13)	56 (17)
\$20 000-\$34 999	58 (16)	57 (17)
\$35 000-\$49 999	62 (17)	54 (16)
\$50 000-\$74,999	85 (24)	82 (25)
\$75,000-\$99,999	48 (13)	38 (11)
≥\$100,000	60 (17)	46 (14)
Education, No. (%) ^b		
< High School	10 (2.7)	7(2.0)
High School or Equivalent	37 (9.8)	49 (14.3)
Some college	148 (39.3)	133 (38.8)
College	109 (28.9)	97 (28.3)
Graduate degree	71 (16.8)	55 (16.0)
Comorbid illness, No. (%) ^c		
Hypertension	254 (68)	239 (70)
Obesity (BMI ≥ 30 kg/m ²)	331 (88)	299 (87)
Arthritis in other joints	209 (55)	178 (52)
Cardiovascular heart disease	40 (11)	35 (10)
Type II Diabetes	70 (19)	78 (23)
Western Ontario and McMaster Universities Osteoarthritic Index (WOMAC) ^d		
WOMAC pain (range 0-20)	7.4 (3.1)	7.4 (3.1)
	25.5 (11.5)	25.5 (11.4)

^aReported on a self-administered demographics questionnaire.

^bSome variables had a small amount of missing data due to refusing to answer the question.

^cReported on a self-administered health history questionnaire as conditions diagnosed by a health care professional. With co-morbid illnesses that could exclude patient from participation, final approval/denial for participation provided after patient evaluation by study physician.

^dThe Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) consists of a self-administered questionnaire including 5 questions on pain, and 17 questions on physical function. Scale for each question ranges from 0 no symptoms to 4 extreme symptoms. Composite scores for pain ranged from 0-20 and for function 0-68. Pain cut points on a 0-20 scale are 2-8, mild, >8 -14, moderate, >14-20 severe (transformed from 0-10 scale reported in (23)).

eTable 2. Comparison baseline values (mean, SD) of completers and non-completers (no follow-up data). The non-completers were younger, heavier, and had more pain and worse function.

	Completers	Non-Completers	P
Age (years)	65.0 (7.7) N = 720	61.9 (7.6) N = 103	<.001
Weight (kg)	100.2 (20.8) N = 720	105.8 (24.3) N = 103	.012
WOMAC Pain (range 0-20)	7.4 (3.1) N = 720	8.4 (3.7) N = 103	.003
WOMAC Function (range 0-68)	25.5 (11.5) N = 720	29.0 (13.5) N = 103	.005

eTable 3. Primary and prespecified secondary outcomes using site as a random effect.

Outcome	Diet + Exercise	Control	Mean difference (95% CI)	^aP value
Primary Outcome				
WOMAC Pain (range, 0-20)				
Baseline mean (SD)	7.4 (3.1) (n = 377)	7.4 (3.1) (n = 316)		
18-month adjusted means (95% CI)	5.0 (4.6 to 5.4) (n = 329)	5.5 (5.1 to 5.9) (n = 316)	-0.6 (-1.0 to -0.1)	.02
Prespecified Secondary Outcomes				
WOMAC Function (range, 0-68)				
Baseline mean (SD)	25.5 (11.5) (n = 377)	25.5 (11.4) (n = 343)		
18-month adjusted means (95% CI)	16.5 (15.3 to 17.7) (n = 325)	19.8 (18.6 to 21.0) (n = 311)	-3.3 (-4.9 to -1.7)	<.001
6-minute walk distance (m)				
Baseline mean (SD)	373 (90) (n = 375)	371 (95) (n = 341)		
18-month adjusted means (95% CI)	419 (411 to 428) (n = 247)	376 (368 to 385) (n = 219)	43 (31 to 54)	<.001
Pain medication use				
Baseline mean (SD)	8.2 (5.0) (n = 377)	8.4 (5.0) (n = 343)		
18-month adjusted means (95% CI)	8.3 (7.9 to 8.8) (n = 231)	8.3 (7.8 to 8.8) (n = 228)	0.0 (-0.5 to 0.5)	0.90
SF-36 Physical (range, 0-100)				
Baseline mean (SD)	34.3 (9.2) (n = 377)	35.9 (9.1) (n = 343)		
18-month adjusted means (95% CI)	41.4 (40.2 to 42.6) (n = 321)	37.6 (36.3 to 38.8) (n = 306)	3.8 (2.5 to 5.2)	<.001
SF-36 Mental (range, 0-100)				
Baseline mean (SD)	55.4 (9.8) (n = 377)	55.0 (9.7) (n = 343)		
18-month adjusted means (95% CI)	55.3 (54.3 to 56.2) (n = 321)	54.1 (53.1 to 55.0) (n = 306)	1.2 (-0.1 to 2.5)	.07

eTable 4. Between-group differences at 18-month follow-up for primary and secondary outcomes using multiple imputation adjusted for baseline body mass index, sex, and baseline values. Weight and waist circumference were not adjusted for baseline body mass index.

Outcome	D+E vs Control (95% CI)	P-value
WOMAC Pain (0-20)	-0.54 (-1.05, -0.04)	.036
WOMAC Function (0-68)	-3.15 (-4.85, -1.45)	.0003
6 Min Walk Distance (m)	42 (29, 55)	<.0001
Weight (kg)	-6.1 (-7.4, -4.8)	<.0001
Waist circumference (cm)	-5.4 (-6.9, -3.8)	<.0001
PASE (0-400)	22 (13, 31)	<.0001
SF-36 Physical (0-100)	3.9 (2.5, 5.3)	<.0001

eTable 5A. Adverse events (AEs) definitely related to the study by group assignment.

Event Description	No. Participants*	(%)**	Events***	No. Participants*	(%)**	Events***
Body Injury	9	2.17	9	1	0.24	1
Muscle Strain	6	1.45	6	1	0.24	1
Leg/Knee Pain	6	1.45	6	0	0.00	0
Trip/Fall	6	1.45	6	0	0.00	0
Dizziness	2	0.48	2	0	0.00	0
Chest Pain	1	0.24	1	0	0.00	0

* -

number of participants experienced AE (participant is to be counted only once for each AE)

** % of total number of participants enrolled

*** - number of events

There were 169 serious adverse events (70, diet and exercise; 99, attention control); none were definitely related to the study. There were 729 adverse events (428, diet and exercise; 301, attention control); 32 (4%) that were definitely related to the study, 10 body injury (9, diet and exercise; 1, attention control), 7 muscle strain (6, diet and exercise; 1, attention control), 6 leg/knee pain, (6 diet and exercise; 0, attention control), 6 trip/fall, (6 diet and exercise; 0, attention control), 2 dizziness, (2 diet and exercise; 0, attention control), 1 chest pain, (1 diet and exercise; 0, attention control).

eTable 5B. Knee replacements and intra-articular knee injections by group assignment.

Event Description	D&E			Control		
	No. Participants*	(%)**	Events***	No. Participants*	(%)**	Events***
Knee Replacement	19	4.59	21	23	5.62	23
Intra-articular Knee Injection	36	8.70	44	56	13.69	75

* - number of participants experienced AE/SAE (participant is to be counted only once for each AE/SAE)

** % of total number of participants enrolled

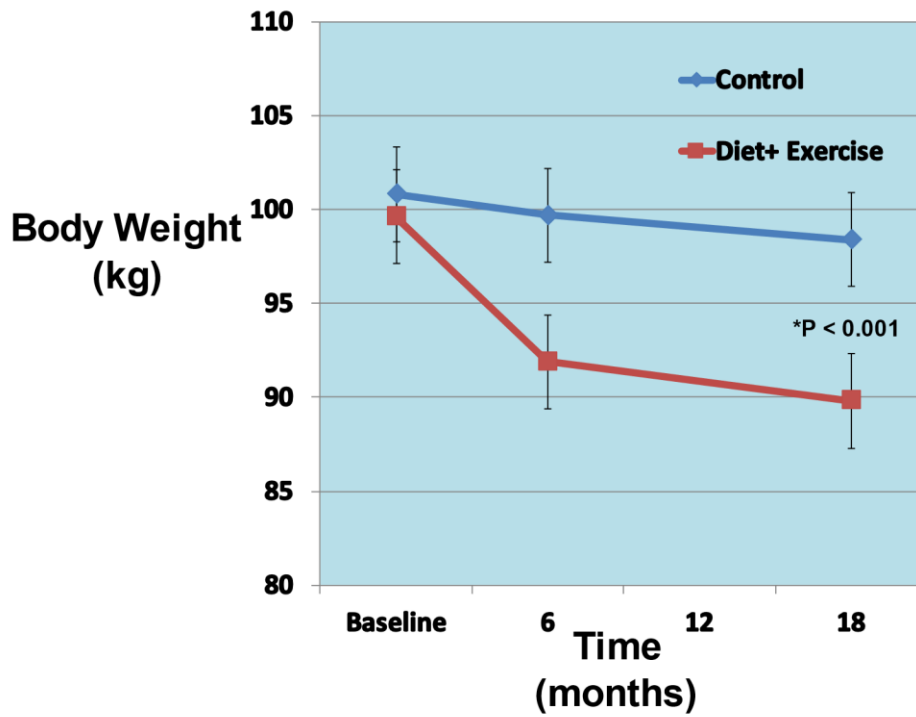
*** - number of events

eTable 6. Comparison of 18-month outcomes with versus without participants (ppts) that were active during COVID

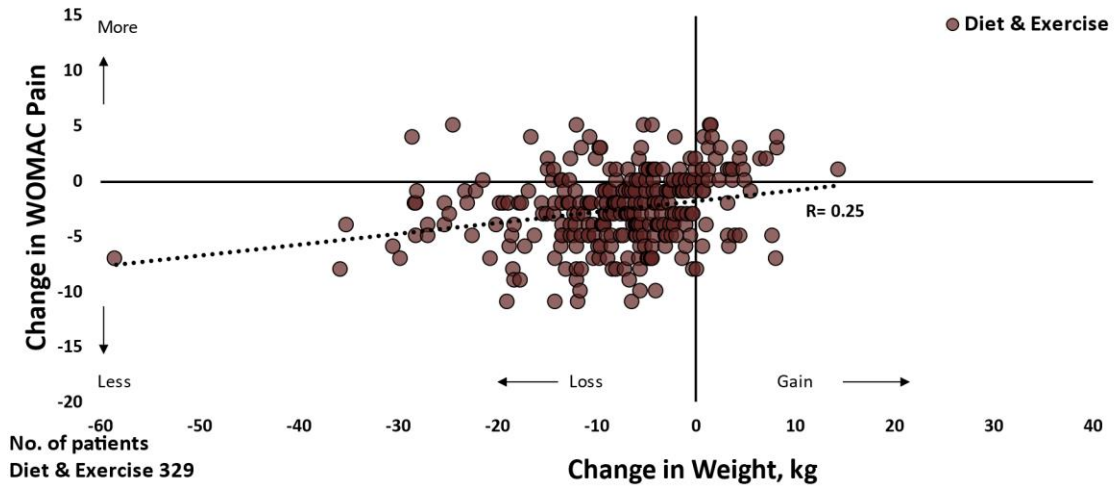
Outcome	Diet + Exercise	Control	Mean difference (95% CI)	P value
WOMAC Pain				
18-month with all ppts	5.0 (4.6 to 5.4) (n = 329)	5.5 (5.1 to 5.9) (n = 316)	-.6 (-1.0 to -0.7)	.02
18-month without COVID ppts	4.8 (4.5 to 5.2) (n = 245)	5.6 (5.2 to 5.9) (n = 252)	-.8 (-1.3 to -.2)	.005
WOMAC Function				
18-month with all ppts	16.5 (15.3 to 17.7) (n = 325)	19.8 (18.6 to 21.0) (n = 311)	-3.3 (-4.9 to -1.7)	<.001
18-month without COVID ppts	16.0 (14.6 to 17.3) (n = 245)	20.1 (18.8 to 21.4) (n = 252)	-4.1 (-5.8 to -2.4)	<.001
6-minute walk distance				
18-month with all ppts	419 (411 to 428) (n = 247)	376 (368 to 385) (n = 219)	43 (31 to 55)	<.001
18-month without COVID ppts	414 (405 to 422) (n = 213)	374 (366 to 383) (n = 209)	39 (28 to 51)	<.001
SF-36 Physical (range, 0-100)				
18-month with all ppts	41.4 (40.2 to 42.6) (n = 321)	37.6 (36.3 to 38.8) (n = 306)	3.8 (2.5 to 5.2)	<.001
18-month without COVID ppts	41.7 (40.6 to 42.8) (n = 244)	37.4 (36.3 to 38.5) (n = 248)	4.4 (2.9 to 5.8)	<.001
SF-36 Mental (range, 0-100)				
18-month with all ppts	55.3 (54.3 to 56.2) (n = 321)	54.1 (53.1 to 55.0) (n = 306)	1.2 (-0.1 to 2.5)	.07
18-month without COVID ppts	55.1 (54.1 to 56.2) (n = 244)	53.9 (52.8 to 55.0) (n = 248)	1.2 (-0.2 to 2.6)	.10

eTable 7. Number and percent of meal replacement use for the diet + exercise and control groups.				
	Diet + Exercise		Control	
	N	%	N	%
6 month follow up				
^a Less than 1x/week	83	26.7	227	82.5
^b 1x or more/week	228	73.3	48	17.5
5-7x/week	113	36.3	22	8.0
12 month follow up				
Less than 1x/week	101	38.8	196	85.6
1x or more /week	159	61.2	33	14.4
5-7x/week	75	28.8	15	6.5
18 month follow up				
Less than 1x/week	148	51.6	202	80.5
1x or more /week	139	48.4	49	19.5
5-7x/week	75	26.1	19	6.6
^a Includes patients in the never, 1x/month, 2-3 x/month categories.				
^b Includes patients in the 5-7x/week category.				

eFigure 1. Mean (95%CI) Unadjusted Body Weight at Baseline and 6 and 18-month Follow-up for Patients for Whom Follow-up Data Were Available.



eFigure 2. Change in Weight vs Change in WOMAC Pain for the Diet and Exercise Group



eFigure 3. Change in Weight vs Change in WOMAC Pain for the Control Group

