

Supplementary Online Content

Messier SP, Mihalko SL, Legault C, 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*. doi:10.1001/jama.2013.277669.

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

eMethods. Knee joint load

Bone-on-bone peak tibiofemoral (knee) compressive force was the primary measure of knee joint loading. A 25-reflective marker set, arranged in the Cleveland Clinic full-body configuration, and a 6-camera Motion Analysis (Santa Rosa, CA) system set to sample data at 60 Hz were used to collect 3-D kinematic data, which were tracked, edited, and smoothed, using EVaRT 4.4 software, and a Butterworth low-pass filter with a cut-off frequency of 6 Hz. The processed data were compiled using OrthoTrak 6.0 β 4 clinical gait analysis software.

A 6-channel force platform (Advanced Mechanical Technologies, Inc., Newton, MA) was integrated with the motion capture system for simultaneous kinetic data collection at 480 Hz. Six successful trials were collected on each participant with 3 chosen for subsequent analysis. A successful trial was defined as one in which the participant's entire foot was placed on the surface area of the force platform while walking within \pm 3.5% of freely chosen speed. The smoothed coordinate data, ground reaction, and gravitational and inertial forces informed an inverse dynamics model to calculate 3-D hip flexion and extension; knee flexion, extension, abduction, internal rotation, and external rotation; and ankle plantar- and dorsiflexion moments.

A musculoskeletal model developed by DeVita and Hortobagyi¹ was used to calculate knee joint compressive force and has two basic components. First, joint moments and joint-reaction forces are calculated from kinematic, physiological, and force-plate data. Then they are used to calculate individual muscle forces and compressive and shear forces in three steps: (1) determining the forces in the gastrocnemius, hamstrings, and quadriceps muscles and lateral support tissues in the knee; (2) applying them along with joint-reaction forces onto the tibia; and (3) determining knee-joint forces. The model, its limitations, and a comparison of its predictions with other models are discussed elsewhere.^{2,3}

Reference List

- (1) Devita P, Hortobagyi T. Functional knee brace alters predicted muscle and joint forces in people with ACL reconstruction during walking. *J Appl Biomech* 2001;17:297-311.
- (2) Messier SP, Legault C, Mihalko S et al. The Intensive Diet and Exercise for Arthritis (IDEA) trial: design and rationale. *BMC Musculoskelet Disord* 2009;10:93.
- (3) Messier SP, Legault C, Loeser RF et al. Does high weight loss in older adults with knee osteoarthritis affect bone-on-bone joint loads and muscle forces during walking? *Osteoarthritis and Cartilage* 2011;19:272-280.

eTable 1. Serious adverse events. All were unrelated to the study.

Serious Adverse Event	Completed Study (Y/N)	Diet	Exercise	Diet + Exercise
Heart Palpitations	Y		X	
ALS	N			X
Stroke	N			X
Lung Hypertension	Y		X	
Lung Infection	Y			X
Cancer	Y			X
Cancer	N	X		
Cancer	Y		X	
Cancer	N			X
Staph Infection	Y			X

eTable 2. Intention-to-treat completers-only analysis. Unadjusted mean (95%CI) mechanistic and clinical outcomes at baseline (0), and 6 and 18-month follow-up by group and 18-month outcomes adjusted for gender, BMI, and baseline values. The adjusted data were used to determine between-group P values and effect sizes. Knee compressive force and IL-6 significance levels were set at 0.025; for secondary outcomes the significance level was 0.05.

	Exercise					Diet					Diet + Exercise					P
	Months – unadjusted				Month 18 adjusted	Months - unadjusted				Month 18 Adjusted [ES]	Months - unadjusted				Month 18 Adjusted [ES]	
	0	6	18	Δ (%)		0	6	18	Δ (%)		0	6	18	Δ (%)		
Comp Force (N)	2816	2946	2662	--154 (-5)	2728	2676	2478	2377	-299 (-11)	2526 [-0.4]	2690	2599	2444	-246 (-9)	2585 [-0.3]	0.019 [#]
95% CI	2657,2975	2800,3092	2513,2810		2622,2834	2509,2843	2326,2629	2224,2531		2417,2634	2528,2852	2454,2744	2296,2592		2479,2690	
N	133	119	111		111	125	109	103		103	134	122	110		111	
IL-6 (pg·mL⁻¹)	2.9	2.9	3.0	0.1 (3)	3.2	3.2	2.7	2.7	-0.5 (16)	2.7 [-0.3]	3.3	2.9	2.8	-0.4 (13)	2.7 [-0.3]	0.0005 [#]
95% CI	2.5, 3.2	2.5, 3.3	2.6, 3.4		2.89,3.51	2.8, 3.6	2.3,3.0	2.3,3.0		2.34,2.97	2.9, 3.7	2.5,3.2	2.4, 3.1		2.39,3.01	
N	133	125	117		117	128	113	114		114	137	129	119		119	
Pain	6.0	4.4	4.3	-1.7 (-28)	4.3	6.4	4.8	4.8	-1.6 (-25)	4.8 [0.2]	6.7	4.6	3.3	-3.4 (-51)	3.3 [-0.4]	0.0001 [†]
95% CI	5.5,6.4	3.8,5.0	3.8,4.9		3.8,4.9	5.9, 6.9	4.2,5.4	4.3, 5.4		4.3,5.3	6.2, 7.3	4.1,5.2	2.7,3.9		2.8,3.8	
N	127	119	127		127	124	115	124		124	138	130	129		129	
Function	22.5	17.2	17.4	-5.1 (-23)	17.2	24.3	18.3	17.8	-7.0 (-29)	17.3 [0.0]	24.5	16.4	13.0	-11.5 (-47)	13.0 [-0.5]	0.0001 [†]
95% CI	20.8,24.3	15.2,19.2	15.4,19.4		15.6,18.8	22.4, 26.2	16.3,20.3	15.8,19.8		15.7,18.8	22.5, 26.6	14.5,18.3	11.1,15.0		11.5,14.6	
N	128	119	127		127	124	116	124		124	138	131	129		129	
WalkSpeed (m·s⁻¹)	1.24	1.33	1.30	0.06 (5)	1.30	1.20	1.26	1.28	0.08 (7)	1.30 [0.0]	1.21	1.32	1.34	0.13 (11)	1.34 [0.3]	0.013 [†]
95% CI	1.21,1.27	1.29,1.36	1.27,1.34		1.28,1.32	1.16, 1.23	1.23,1.29	1.25,1.32		1.28,1.32	1.18, 1.24	1.29,1.36	1.30,1.37		1.32,1.36	
N	128	121	108		108	124	112	111		111	138	132	117		117	
6 minute walk (m)	483	538	528	45 (9)	530	481	505	502	21 (4)	499 [-0.5]	466	538	541	75 (16)	548 [0.3]	<0.0001 [‡]
95% CI	468,499	528,553	513,544		519,541	468, 495	489,520	487,518		489,510	451-481	523,553	526,556		537,558	
N	127	118	106		106	124	109	107		107	137	129	116		116	
SF-36 Physical	37.3	41.6	42.4	5 (13)	43.1	36.2	42.1	42.2	6 (17)	42.5 [-0.2]	36.3	43.4	45.1	9 (25)	44.8 [-0.0]	0.054
95% CI	35.7,38.9	39.8,43.3	40.6,44.2		41.6,44.5	34.6, 37.9	40.3,43.8	40.5,45.0		41.1,43.9	34.8, 37.9	41.8,45.1	43.4,46.8		43.5,46.2	
N	127	118	121		121	122	112	124		124	137	131	124		124	
SF-36 Mental	56.7	56.2	55.4	-1.3 (-2)	55.8	56.4	55.0	55.1	-1.0 (-2)	55.5 [-0.1]	57.5	57.2	56.5	-1.0 (-2)	56.0 [0.2]	0.863
95% CI	55.3,58.0	54.8,57.6	54.0,56.9		54.5,57.0	55.0, 57.9	53.6,56.5	53.7,56.6		54.3,56.7	56.4, 58.5	55.9,58.5	55.1,57.9		54.7,57.2	
N	127	118	121		121	122	112	124		124	137	131	124		124	

Δ = 18-month follow-up minus baseline for participants that completed the study (i.e., returned for 18-month testing)

ES = Effect size compared to Exercise-only group

[#]D+E and D < E; ^{*}D+E<E and D; [†]D+E>E and D; [‡]D+E>E and D, E>D. All P values and ES based on 18-month adjusted means.

For more detail on pairwise comparisons see eTable 3.

eTable 3. Intention-to-treat completers-only analysis. Pairwise between group differences (mean and 95% CI) at 18-month follow-up for primary and secondary outcomes. Knee compressive force and IL-6 t-tests were set at a 0.008 significance level; for secondary outcomes the significance level was 0.0167.

	Exercise vs. Diet	p	Exercise vs. Diet + Exercise	p	Diet vs. Diet + Exercise	p
Knee Comp Force N	202 (56, 348)	0.007	142 (1, 285)	0.05	-60 (-205, 86)	0.42
IL-6 pg·mL⁻¹	0.54 (0.11, 0.98)	0.0007*	0.50 (0.07, 0.93)	0.0007*	-0.05 (-0.48, 0.38)	0.97*
Pain	0.43 (-1.15, 0.29)	0.24	1.05 (0.33, 1.78)	0.004	1.48 (0.78, 2.18)	< 0.0001
Function	0.04 (-2.31, 2.24)	0.97	4.21 (1.93, 6.49)	0.0003	4.25 (2.04, 6.45)	0.0002
Walk Speed (m·s⁻¹)	0.00 (-0.03, 0.03)	0.92	-0.04 (-0.07, -0.01)	0.01	-0.04 (-0.07, -0.01)	0.009
6 minute walk (m)	30.5 (15.2, 45.9)	0.0001	-17.8 (-33.1, -2.6)	0.02	-48.3 (-63.1, -33.6)	<0.0001
SF-36 Physical	0.55 (-1.48, 2.58)	0.60	-1.78 (-3.82, 0.25)	0.09	-2.33 (-4.29, -0.36)	0.02
SF-36 Mental	0.26 (-1.54, 2.06)	0.78	-0.22 (-2.04, 1.59)	0.81	-0.48 (-2.23, 1.27)	0.59

*p-value from the log-adjusted variable comparisons.

eTable 4. Mean (95% CI) dose response to weight change with knee compressive force, IL-6, pain, and function independent of group assignment.

% Weight Change	Compressive Force (N)	IL-6 (pg·ml⁻¹)	Pain	Function
High -32.5% to -10.1%	2482 (2397, 2568)	2.64 (2.42, 2.87)	3.72 (3.17, 4.27)	13.27 (11.54, 15.00)
Medium -9.8% to -5.0%	2708 (2616, 2799)	2.75 (2.48, 3.03)	4.62 (4.05, 5.19)	16.46 (14.75, 18.17)
Low -4.9% to 9.9%	2842 (2772, 2911)	3.07 (2.86, 3.28)	4.33 (3.88, 4.78)	17.17 (15.81, 18.53)
P value	<0.001	0.02	0.02	0.01

eFigure. Mean (95%CI) month-by-month weight loss of the D and D+E groups. If a participant was absent on weigh-in day the weight from the previous month was carried forward for that month.

