Effects of Exercise and Diet in Osteoarthritis

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OA Research Team













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Supported by the





Prevalence of Knee Osteoarthritis Worldwide



Vos et al. Lancet, 2012

How we treat Knee OA



Average duration (years) of non-surgical regimen or prosthesis survival

Adapted from Losina, ACR Annual Meeting, 2011

Proportion who ever received treatment (%)



162% rise in knee replacement surgery over the past 20 years

Primary and Revision Total Knee Arthroplasty Medicare Volume Between 1991 and 2010



A cost of \$5 billion annually

Cram et al., JAMA, 2012

Odds Ratio of Knee OA with Obesity for Women



Odds Ratio

Risk of Premature Death is related to Overweight and Obesity

From: Excess Deaths Associated With Underweight, Overweight, and Obesity

Adapted from: JAMA. 2005;293(15):1861-1867. doi:10.1001/jama.293.15.1861





How Can We Reduce Weight and Relieve Pain?





Anti-Obesity Weight Loss Pill

 "Obesity Society President Patrick O'Neil said he's encouraged by the drug's approval because it underscores the notion that lifestyle changes alone are not enough to treat obesity"

AP: June 28, 2012

ears HI)A Belviq expected in 2013; test results described as modest BY MATTHEW PERRONE The Associated Press WASHINGTON - The Food and Drug Administration has approved Arena Pharmaceutical's anti-obesity pill Belvig, the first new prescription drug for long-term weight loss to enter the U.S. market in more

Weight Reduction



Roux-en-Y Gastric Bypass Surgery





Moseley et al. NEJM, 2002

Treatments of Chronic Non-Cancer Pain

- a general conclusion is that the results are sobering. Turk et al., Lancet. 2011
- the best evidence for pain reduction averages roughly 30% in about half of treated patients

Can A Non-Pharmacologic, Non-Invasive Intervention Be Part of the Solution?







NIAMS: R01-AR052528-01

OVER 25 YEARS OF REDUCING KNEE PAIN IN OLDER ADULTS WITH EXERCISE AND DIET

1991-1996: Fitness Arthritis in Seniors Trial (FAST)

1997-2002: Arthritis Diet and Activity Promotion Trial (ADAPT)

2006-2011: Intensive Diet and Exercise for Arthritis (IDEA)

2011-Present: Strength Training for ARthritis Trial (START)

FITNESS ARTHRITIS AND SENIORS TRIAL

Wake Forest University University of Tennessee, Memphis







Intensive Diet and Exercise for Arthritis (IDEA): A Plan for Action

Messier, S.P., Mihalko, S., Nicklas, B., Legault, C., Miller, G.D., DeVita, P., Hunter, D.J., Eckstein, F., Guermazi, A., Williamson, J.D., Carr, J., Beavers, D., Lyles, M., Loeser, R.







NIAMS: R01-AR052528-01



IDEA Intervention Groups



Intensive

Dietary Restriction

IDEA Exercise Intervention





IDEA Nutrition Intervention

- Initial energy intake deficit of 800-1000 kcals/day
- Up to 2 meal replacements (300 kcals each) per day
- GNC Lean Shakes
- Third meal between 500-750 kcals (low in fat)
- Weight loss goal: ≥10% body weight over 18 months
- Meetings: weekly/0-6 months
- Biweekly/7-18 months



IDEA Participant Progress



EXERCISE ADHERENCE (intent-to-treat)

0-6 months: 66% 0-18 months: 54%



Exercise-only

0-6 months: 70% 0-18 months: 58%



Diet + Exercise



DIET ADHERENCE (intent-to-treat)

0-18 months: 63%

0-18 months: 61%



Diet-only



Diet + Exercise



IDEA Adverse Events

454 participants; 18-month Exercise/Diet interventions

3 nonserious adverse events (<1%) 1- muscle strain 2- trips/falls

No serious adverse events related to the study

No deaths

Weight Change



Group	Time	Mean (kg)	Change (kg)	% Change
Diet	base	93.4		
	FU6	85.5	-7.9	8.5
	FU18	84.5	-8.9	9.5
Diet+ Exer	base	93.0		
	FU6	84.3	-8.7	9.4
	FU18	82.4	-10.6	11.4
Exer	base	92.3		
	FU6	92.4	+0.1	0
	FU18	90.5	-1.8	2.0







Lean and Fat Mass Change

Group	Time	Body Wt (kg)	Δ (kg)	Lean, kg	Δ (kg)	Fat, kg	Δ (kg)
Diet	base	93.4		55.3		36.3	
	FU18	84.5	-8.9	51.1	-4.2	31.5	-4.8
Diet+Exer	base	93.0		55.6		36.8	
	FU18	82.4	-10.6	50.8	-4.7	30.3	-6.5

D+E: 61% of wt loss was fat D: 54% of wt loss was fat loss

Pain vs. Time [mean (SE)]



*Adjusted for gender, BMI, baseline values

Mean (SE) WOMAC Function vs. Time



Mean (SE) Walk Speed



Messier et al., JAMA, 2013

Mean (SE) 6 Minute Walk Distance



Messier et al., JAMA, 2013

Musculoskeletal Model Vodel



Blood Biomarkers

<u>Blood Collection</u>: Blood drawn after overnight fast in absence of symptoms of infection/injury

Blood assays: All samples measured in duplicate, average used for data analyses

- <u>Plasma IL-6</u>: Quantikine[®] high-sensitivity ELISA (R&D Systems; sensitivity>0.10 pg/mL, detection range=0.156-10.0 pg/mL)
- <u>Serum Leptin</u>: Quantikine[®] high-sensitivity ELISA (R&D Systems
- <u>Serum MMP-3</u>: Quantikine DMP300 kit

Knee Compressive Force(N)



*Adjusted for gender, baseline BMI, baseline values

Messier et al., JAMA, 2013

IL-6 (pg/mL)



Messier et al., JAMA, 2013





Dose response of weight change with pain and function independent of group assignment

% Weight Change		Pain		Function	
	Ν		P- Value	Month	P- Value
High -32.5% to -10.1%	112	3.72 (0.25)		14.32 (0.77)	
Medium -9.8% to -5.0%	79	4.55 (0.21)	0.02	16.97 (0.68)	0.01
Low -4.9% to 9.9%	165	4.61 (0.19)		17.36 (0.60)	

Adjusted for intervention, BMI, gender and baseline values High < Medium and Low



Adjusted for baseline values, group, baseline BMI, gender

Mean IL-6 (pg/mL) by Weight Loss Category



Weight Loss Category

Adjusted for baseline values, group, baseline BMI, gender

Conclusion

 On average, our D+E intervention was twice as effective at relieving pain as previous long-term OA trials and twice as effective as non-pharmacologic trials of chronic non-cancer pain generally.



Summary

- Intensive weight loss significantly impacts both the biomechanical and inflammatory OA disease pathways
- by reducing knee joint compressive loads
- and inflammation



IDEA: Mechanistic Changes and Clinical Improvements

Intensive Weight Loss + Exercise

Reduces Abnormal Stress

Decreased Joint Loads Reduces Abnormal Physiology Lowers Inflammation

Less Pain Less Disability

Summary

- There was a significant dose response to weight loss.
- 10% weight loss resulted in superior results relative to 5-10%, and less than 5% weight loss.





Can physicians help?

•Only 42% older obese adults who visit doctor are advised to lose weight (Galuska et al, JAMA, 1999)

•What's worse: only 0.7 minutes (42 seconds) are spent discussing diet or exercise. (Flocke, Stange, Prev Med., 2004)



Future of weight loss and exercise interventions

People need help and regular attention to succeed



