



CARDIOMETABOLIC HEALTH CONGRESS

March 4-5, 2016 • San Francisco, CA

# Progressive Approaches to Obesity Management: Integrating Diet, Exercise and Pharmacotherapies

**Samuel Klein, MD**

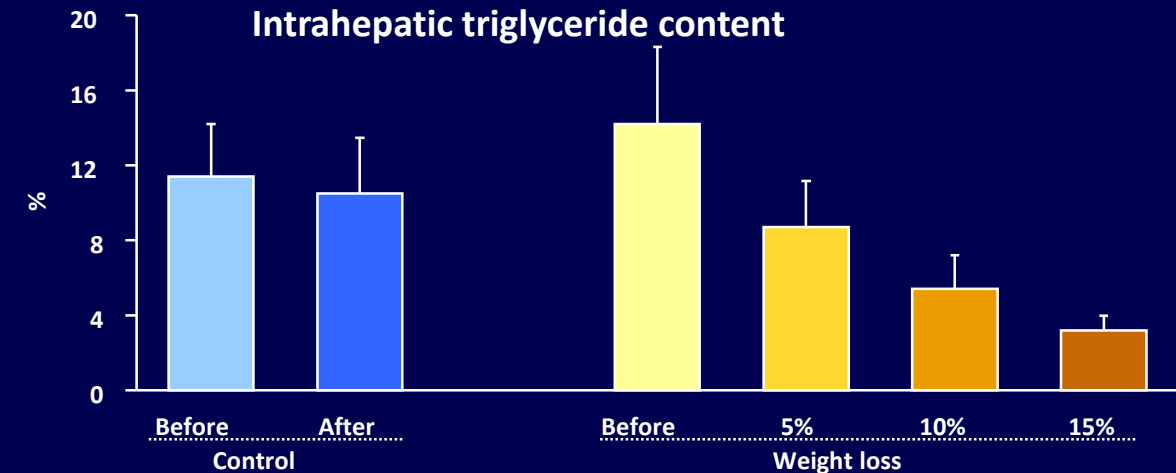
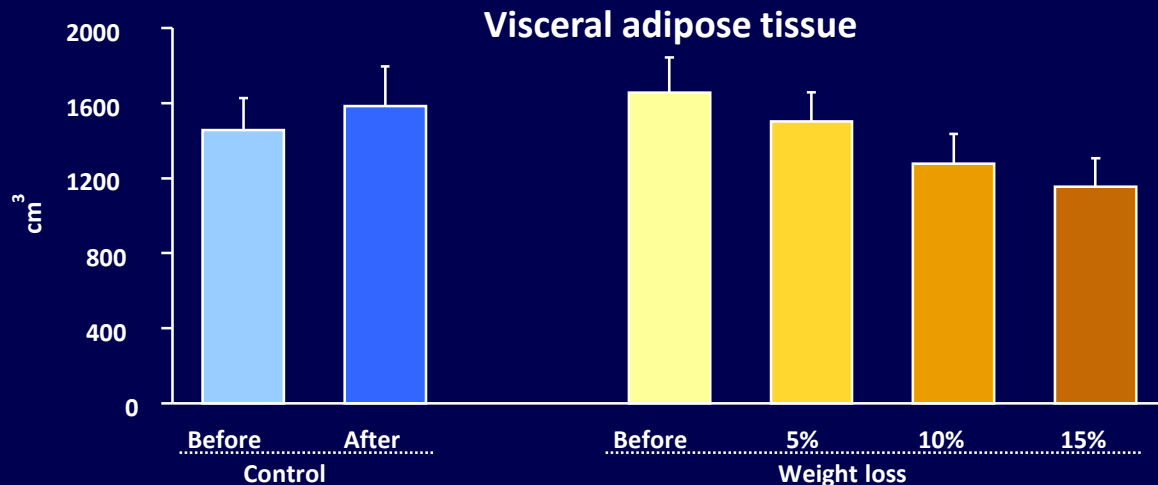
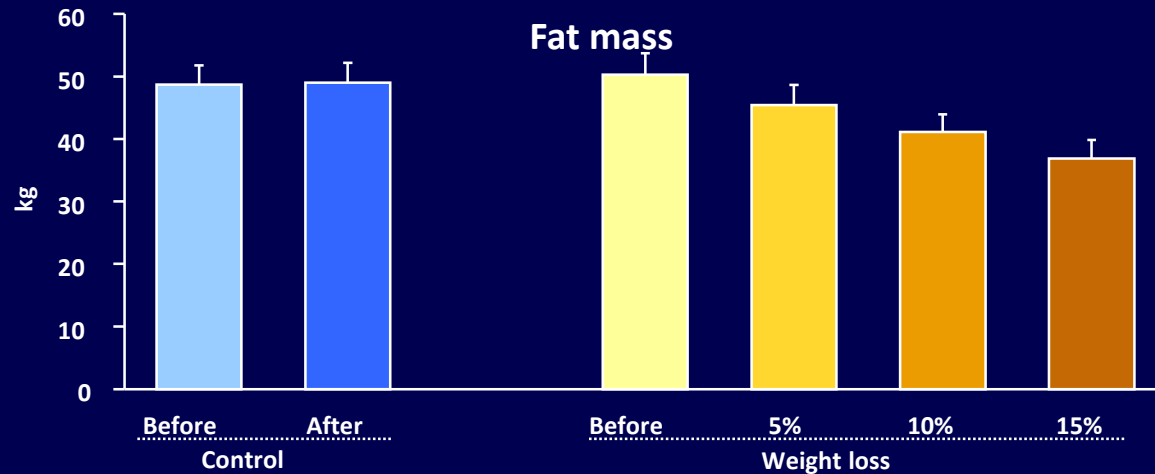
*William H. Danforth Professor of Medicine and Nutritional Science*

*Chief, Division of Geriatrics and Nutritional Sciences*

*Director, Center for Human Nutrition Washington University School of Medicine*

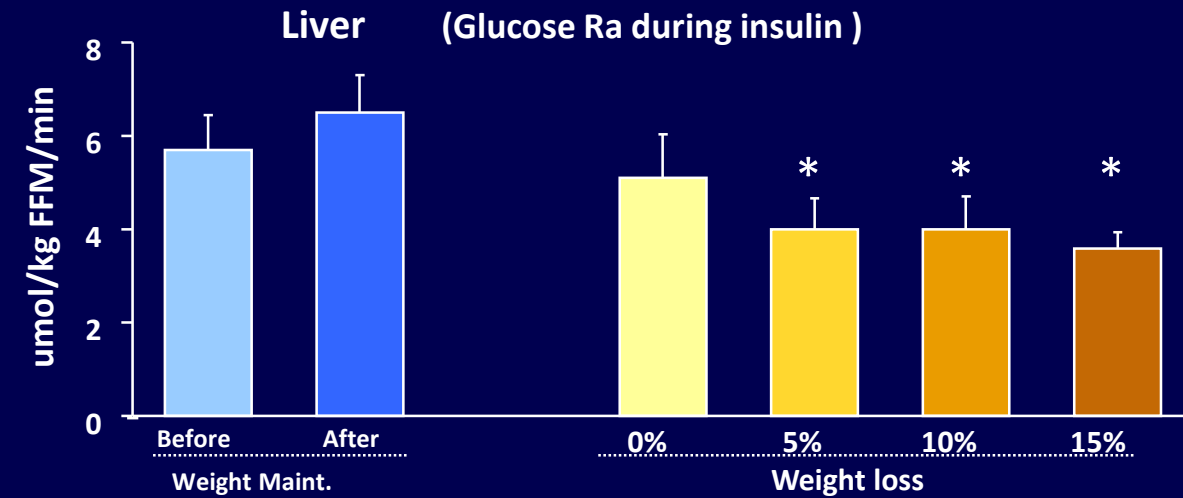
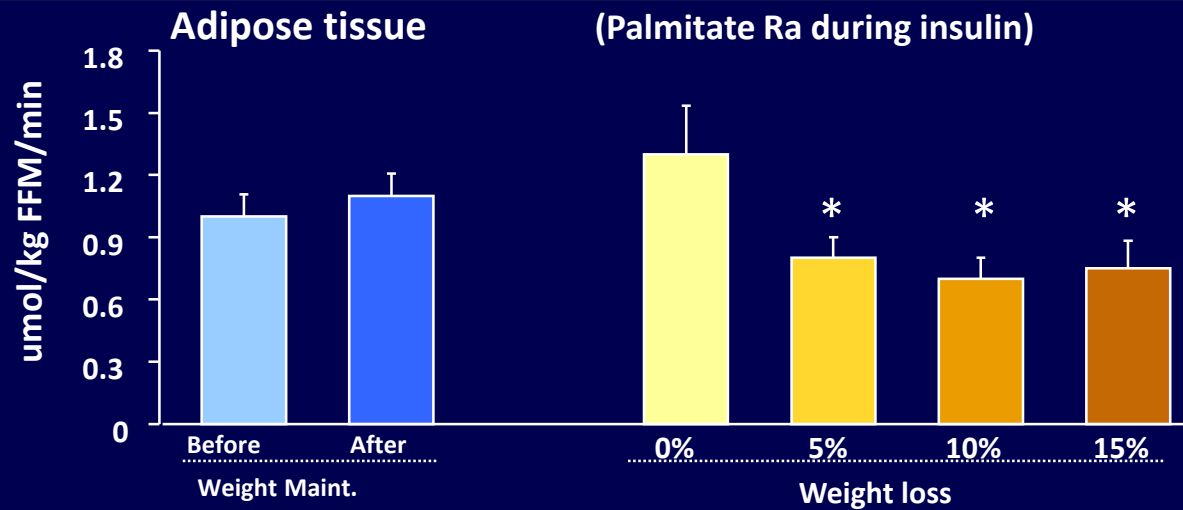
*St. Louis, MO*

# Effect of Progressive Weight Loss on Body Composition

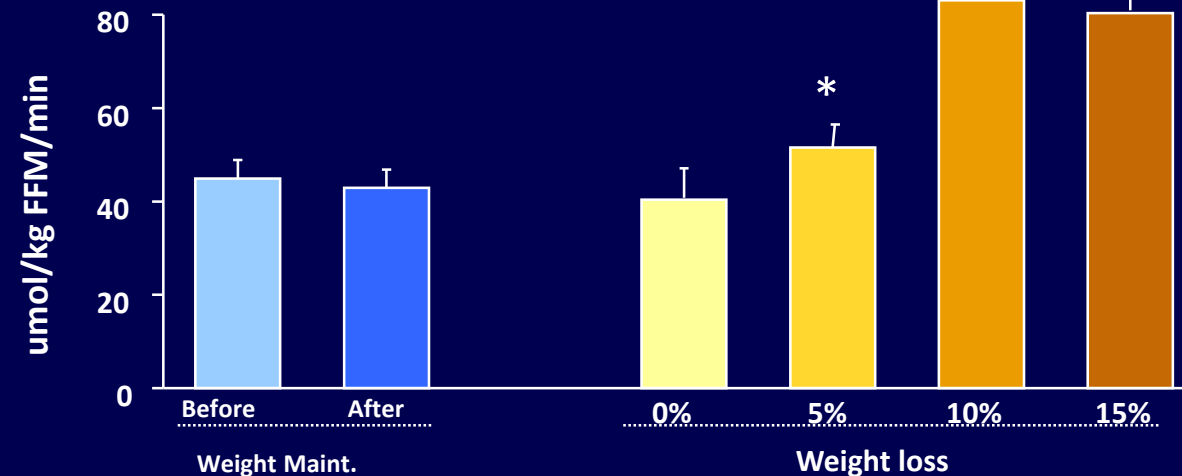


Magkos F et al. *Cell Metab* 2016

# Progressive Weight Loss and Multi-organ Insulin Sensitivity

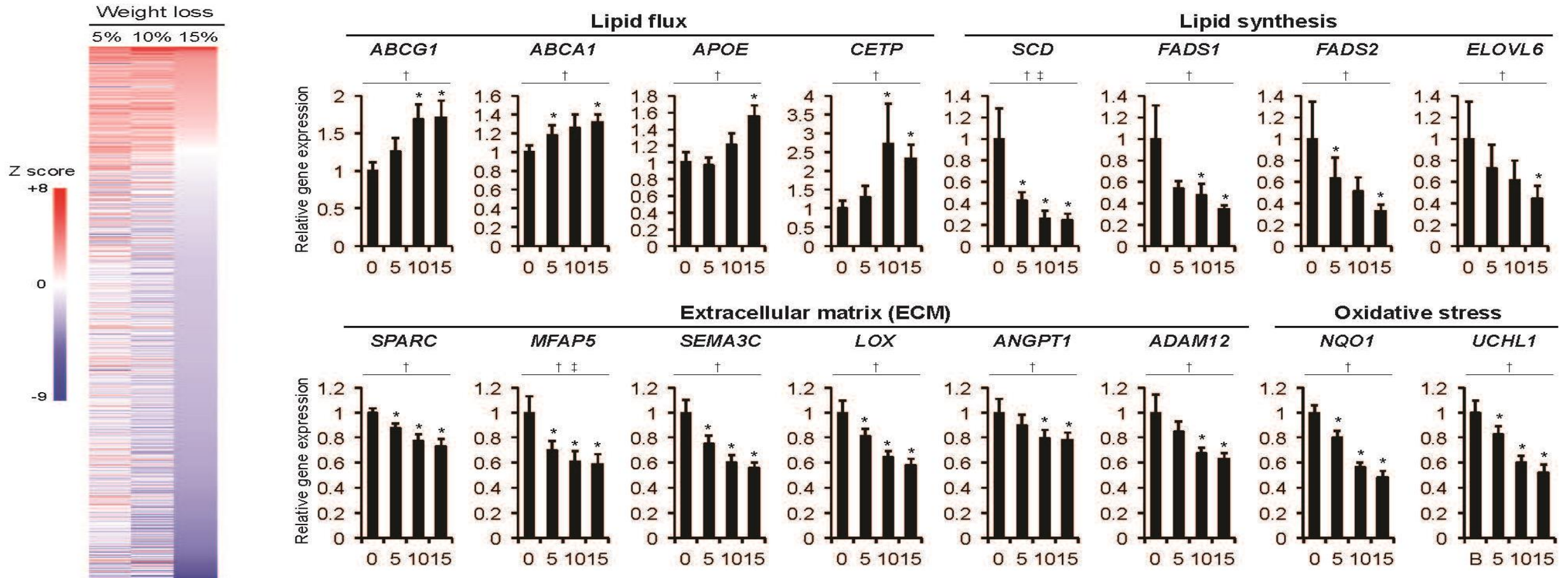


**Skeletal muscle**  
(Glucose Rd during insulin)

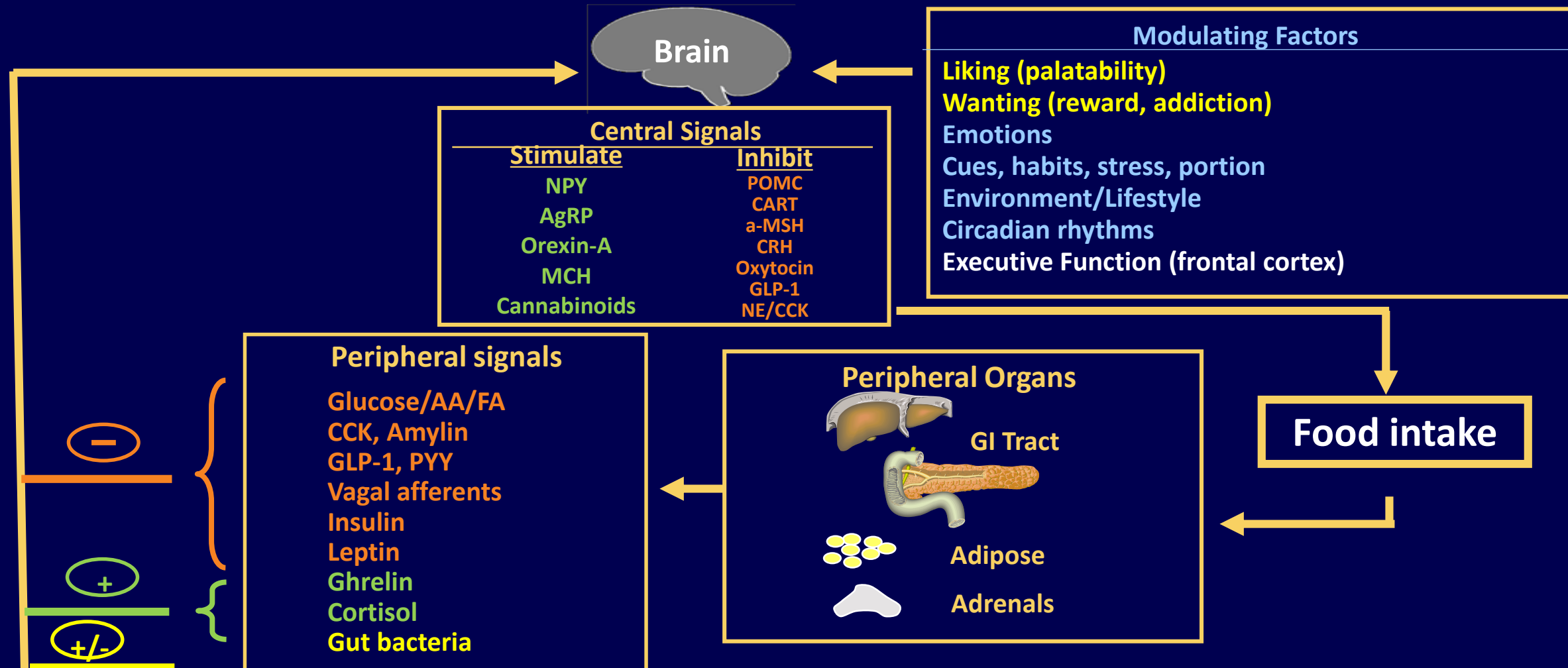


\*P<0.05 vs 0%  
Magkos F et al. *Cell Metab* 2016

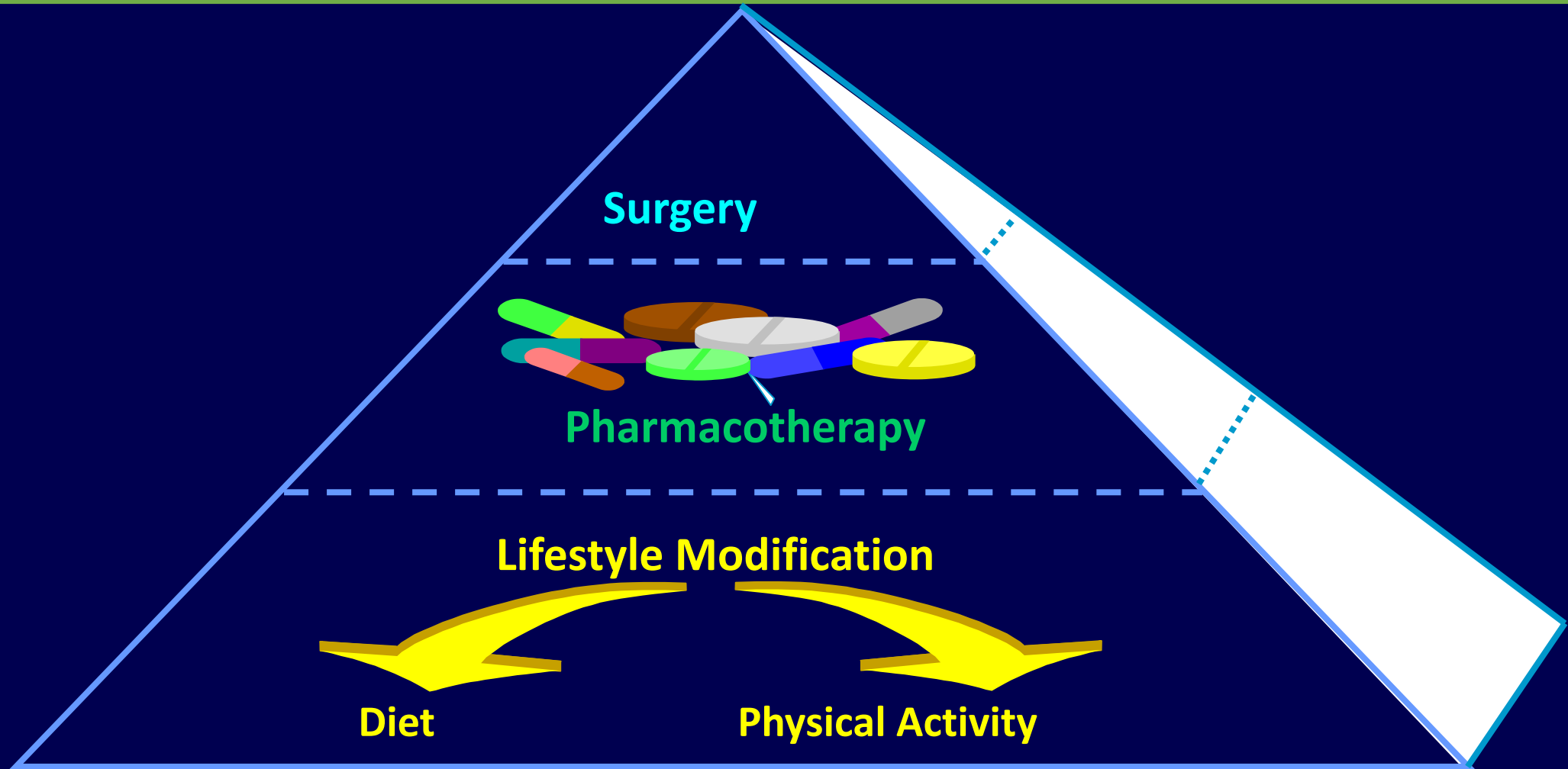
# Effect of Progressive Weight Loss on Adipose Tissue Gene Expression



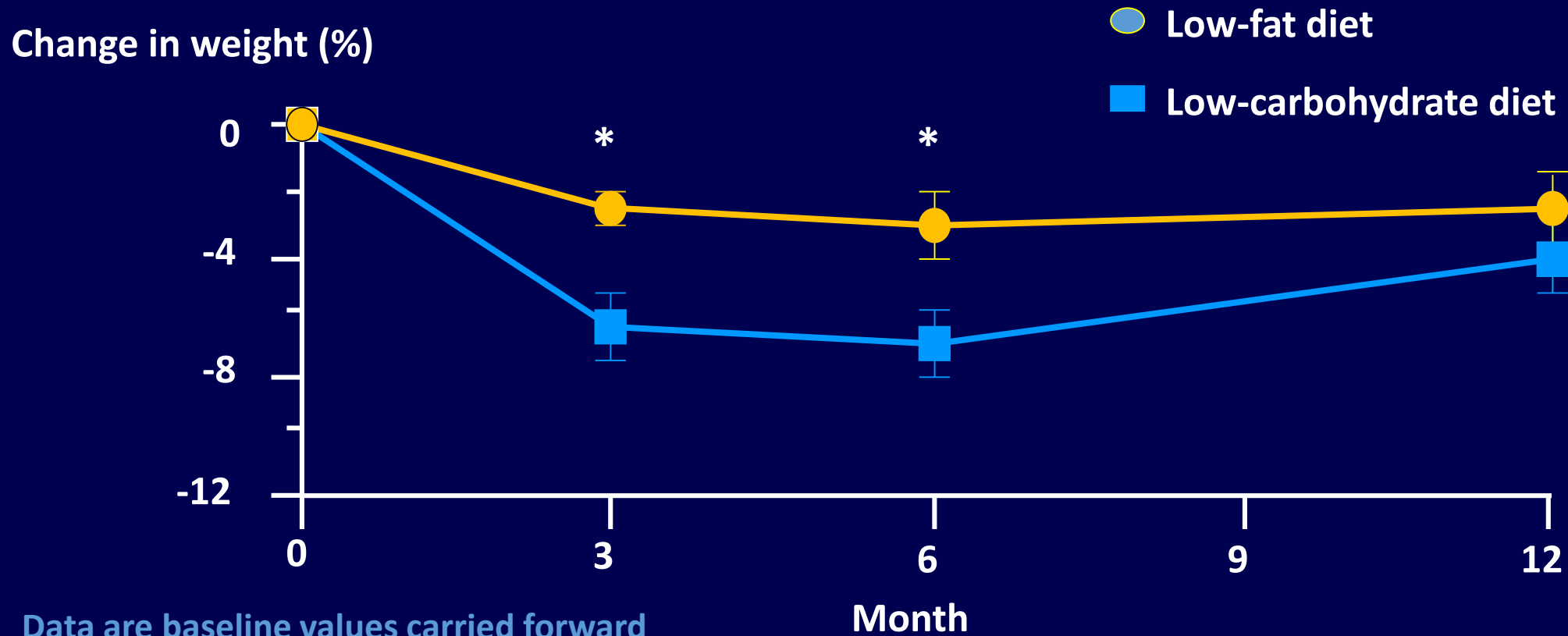
# Regulation of Food Intake



# Obesity Treatment Pyramid



# Effect of Low-Carbohydrate vs Low-Fat Diet on Body Weight



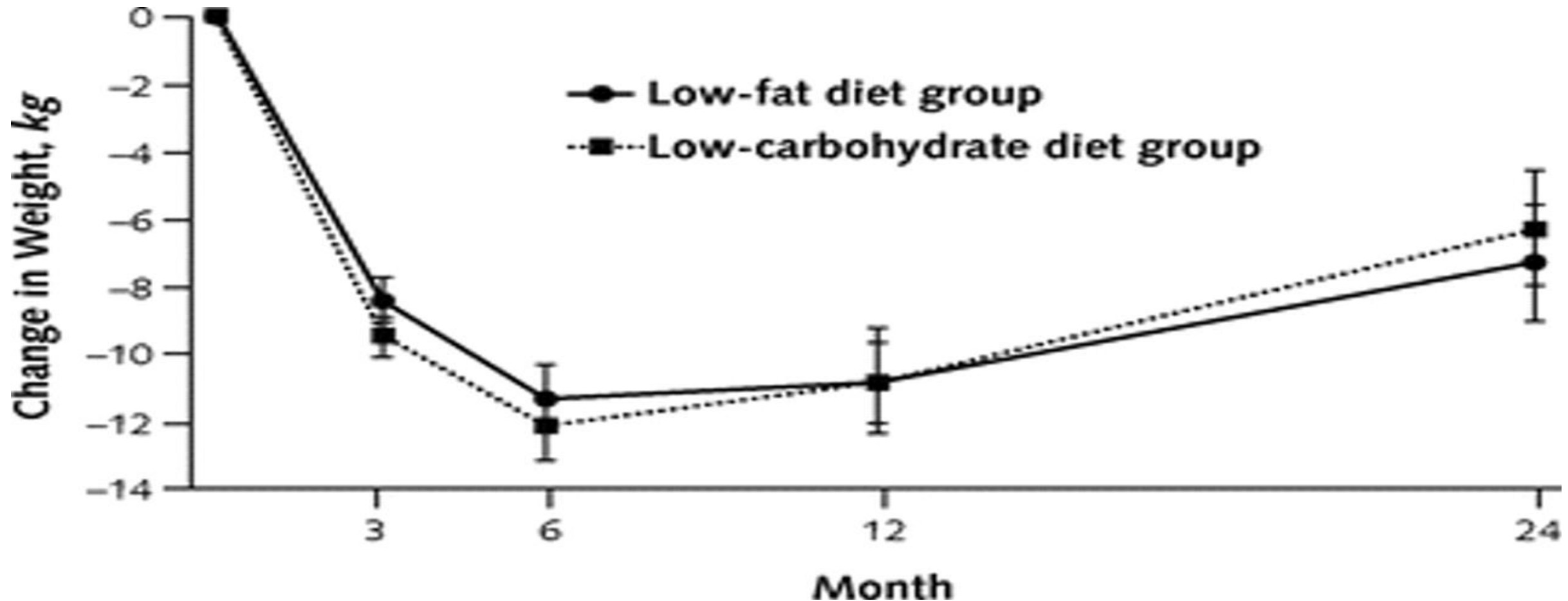
\* $p < 0.05$

Foster et. al. *N Engl J Med* 2003;348:2082.

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# Effect of Low-Carbohydrate vs Low-fat Diet on Body Weight

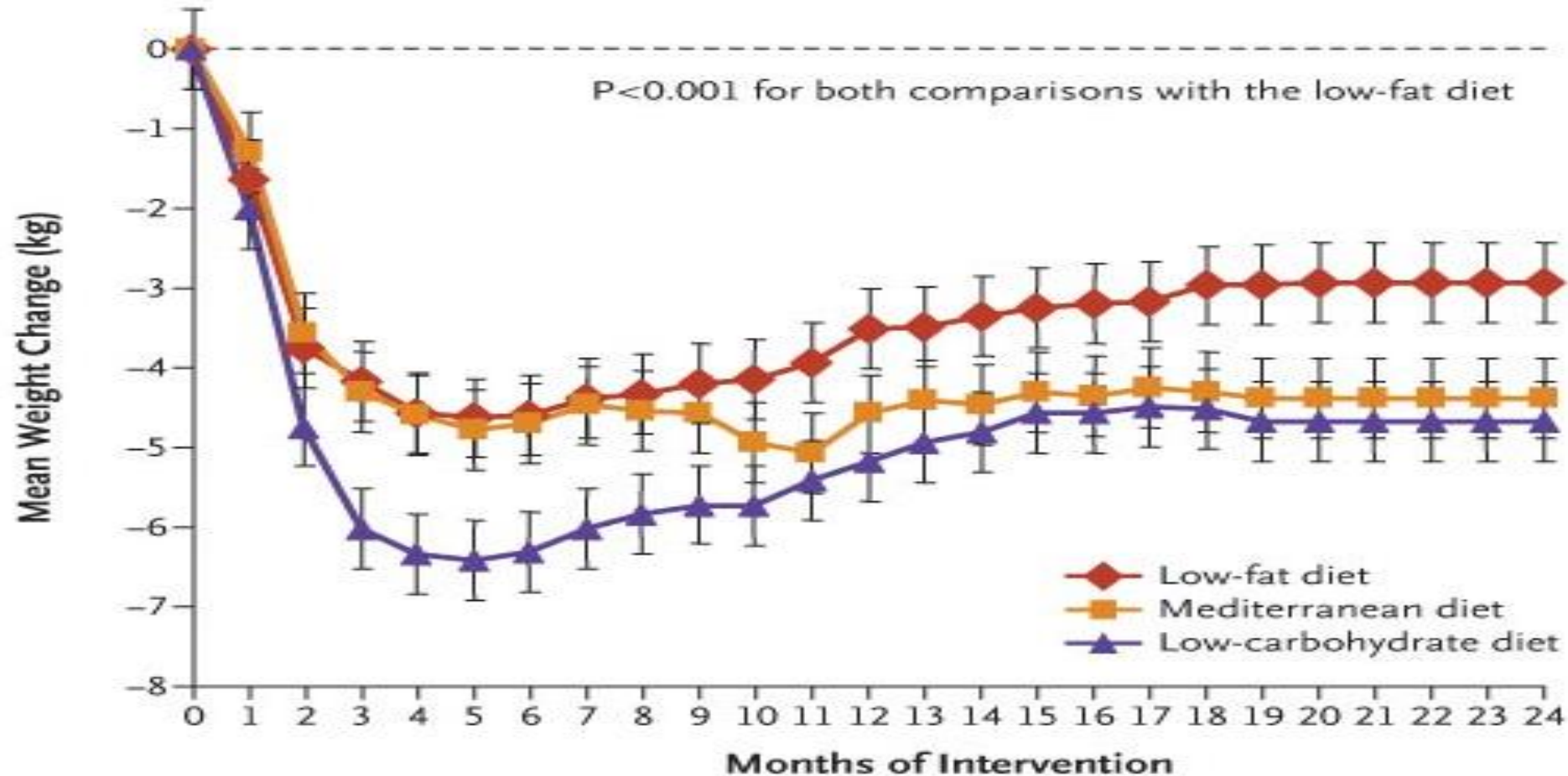


Foster G. et. al. *Ann Intern Med* 2010;153:147.

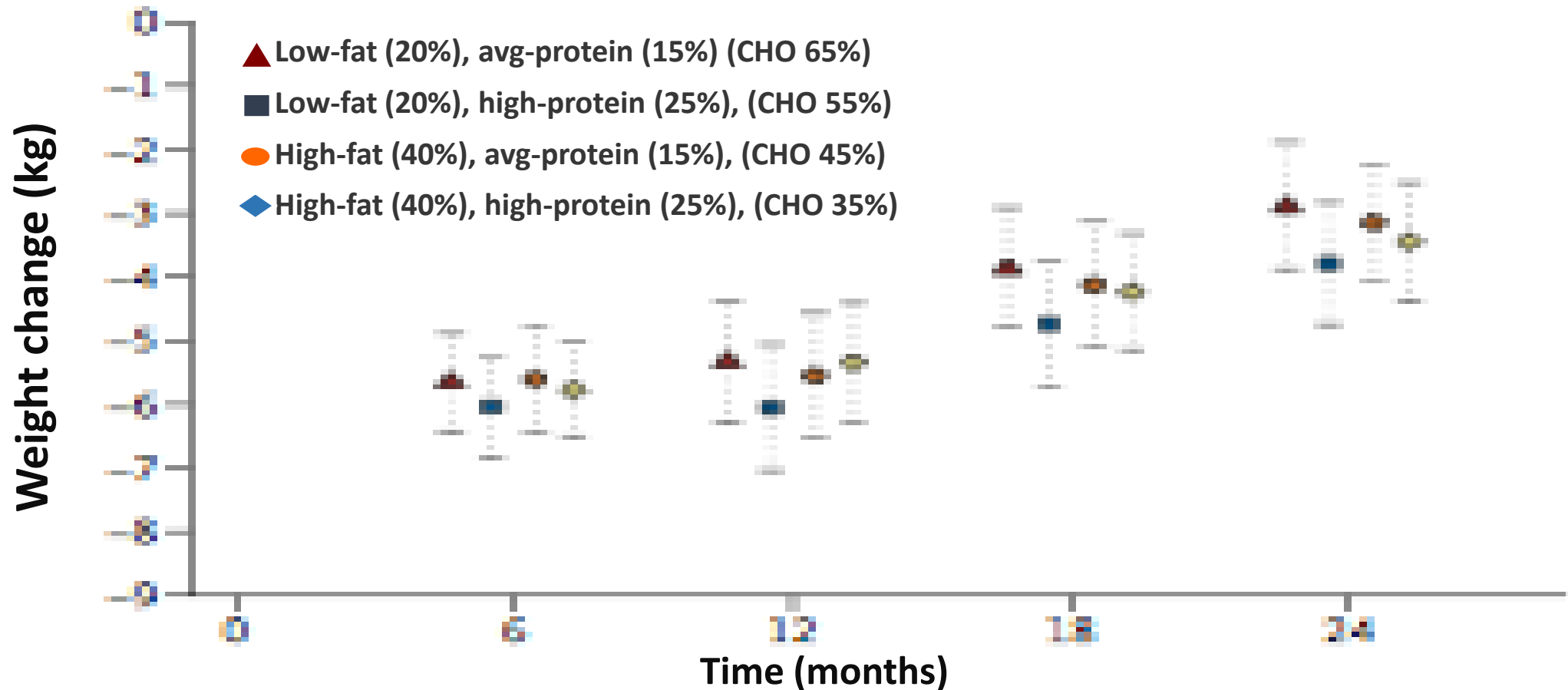
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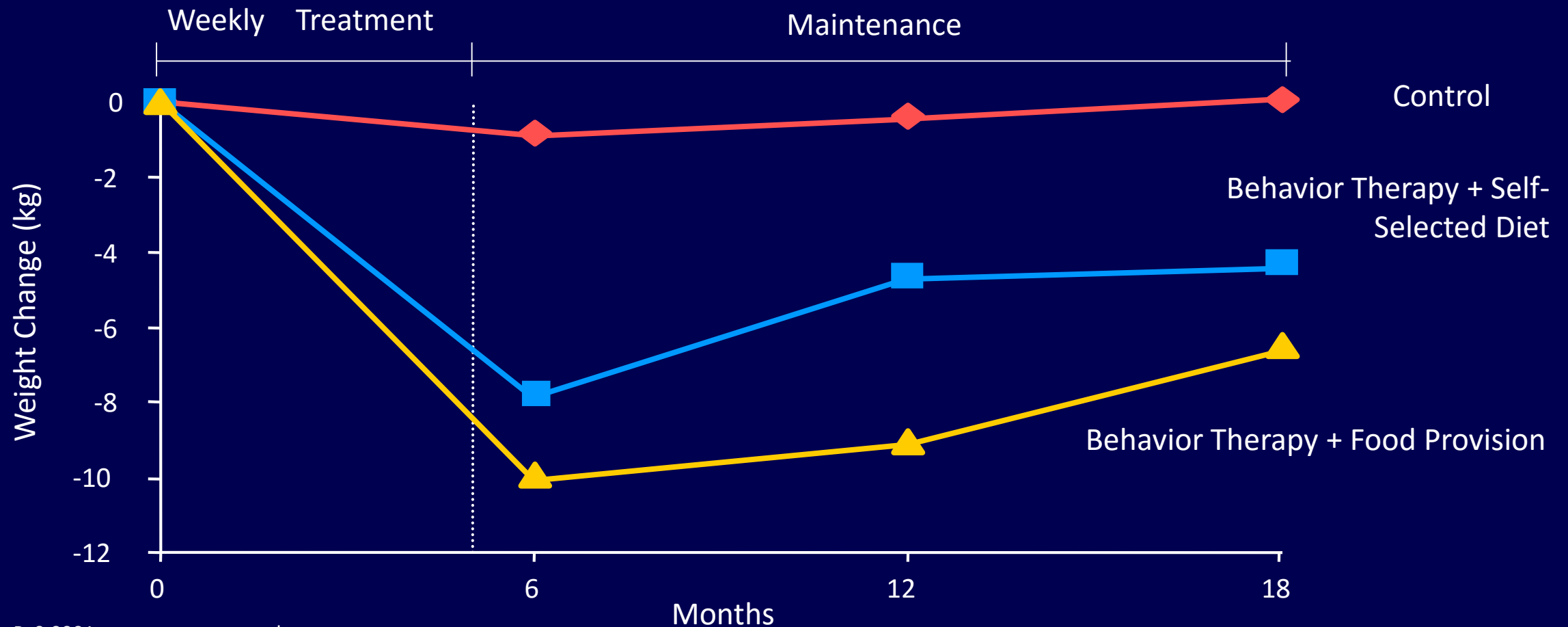
# Effect of Dietary Macronutrient Composition on Weight Loss



# Effect of Dietary Macronutrient Composition on Weight Loss



# Providing Prepackaged Meals Enhances Weight Loss

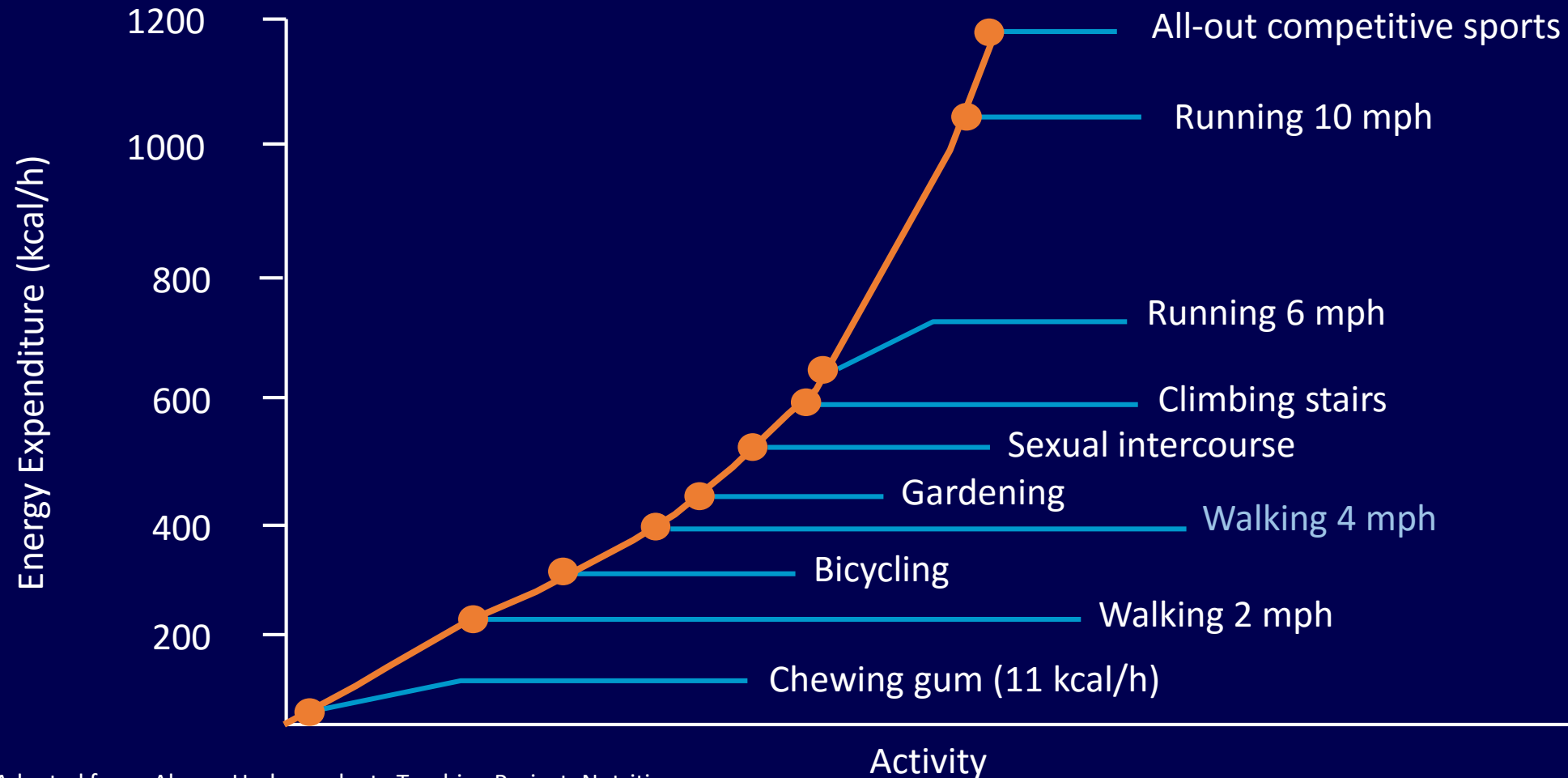


$P=0.0001$  treatment vs control.

$P=0.0002$  behavior therapy + self-selected diet vs behavior therapy + food provision.

Jeffery et al. *J Consult Clin Psychol* 1993;61:1038.

# Energy Expenditure of Physical Activity



Adapted from: Alpers. Undergraduate Teaching Project. Nutrition: energy and protein. American Gastroenterological Association, 1978.

# To Achieve a 300 kcal Negative Energy Balance:

Reduce intake by:

Eliminating  
2 oz potato chips



or

Substituting 2 diet  
sodas for 2 regular  
sodas



Or increase activity by:

Running 3 miles in 30  
min



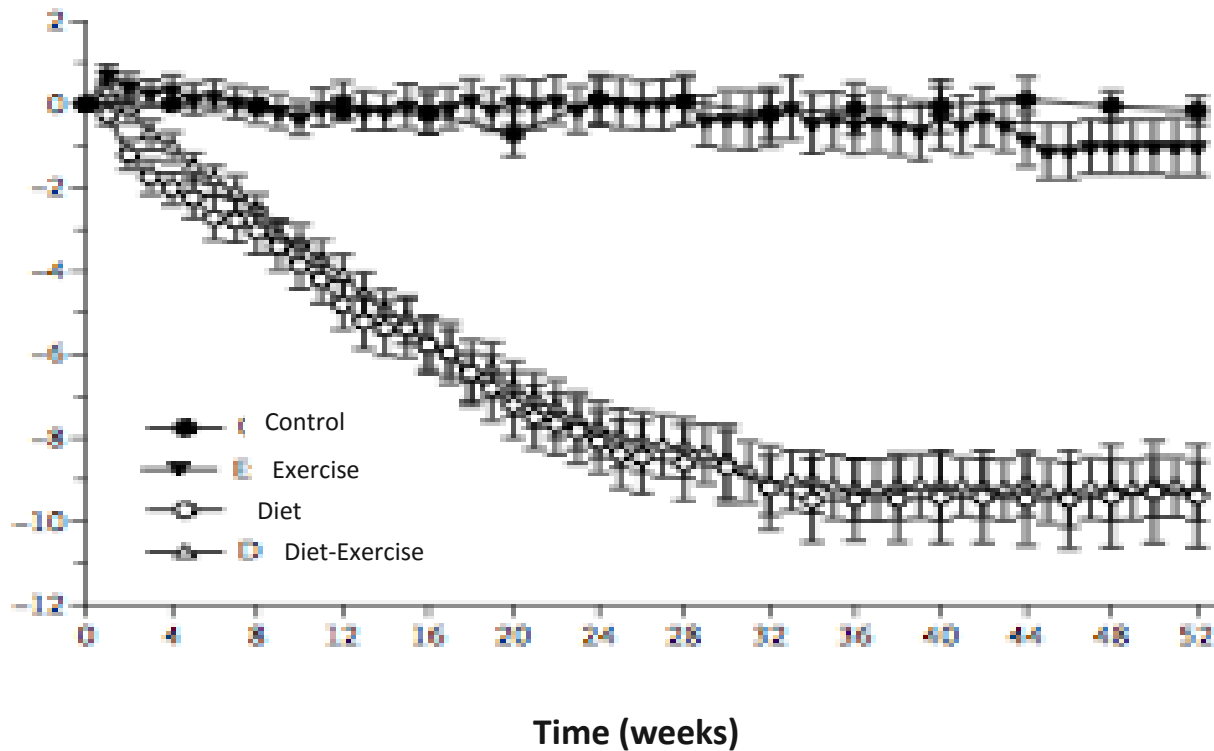
or

Bicycling 8 miles in 30 min

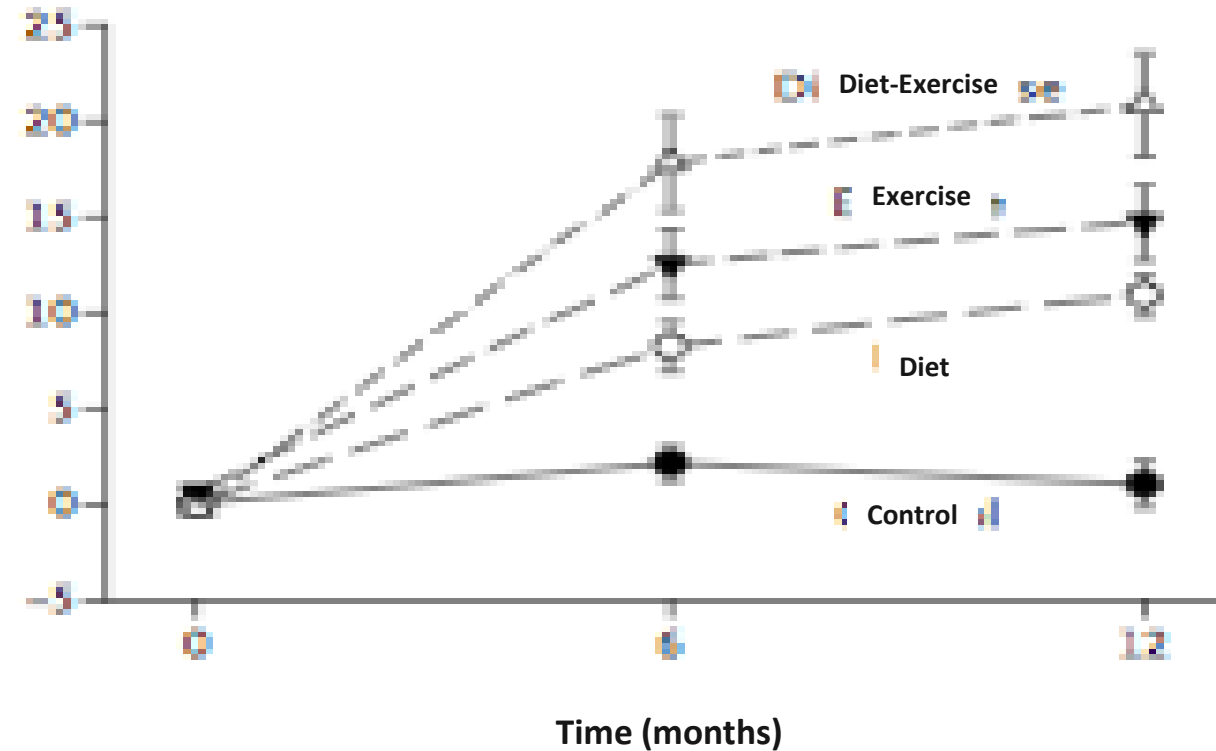


# Effect of Weight Loss $\pm$ Exercise on Physical Function in Obese Older Adults

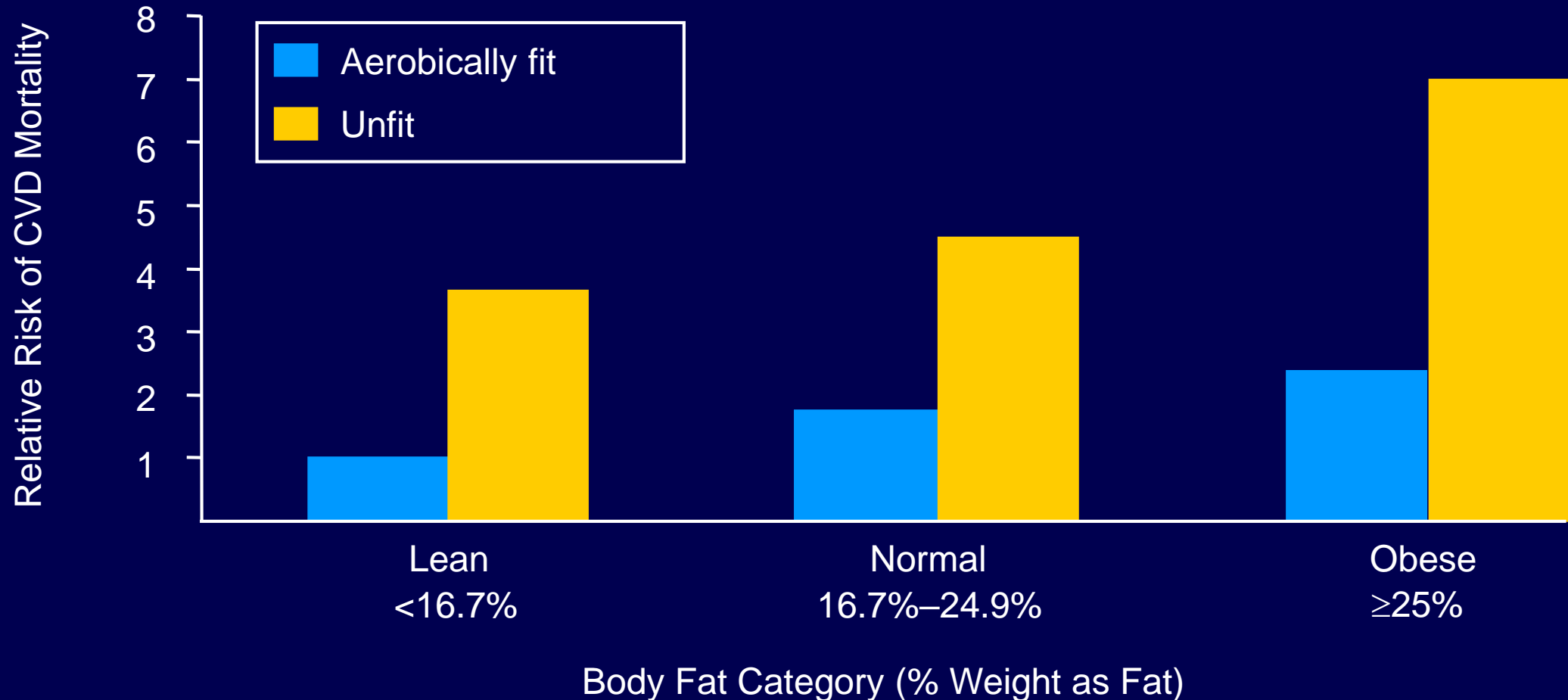
Change in Weight (%)



Change in Physical Performance Test Score (%)



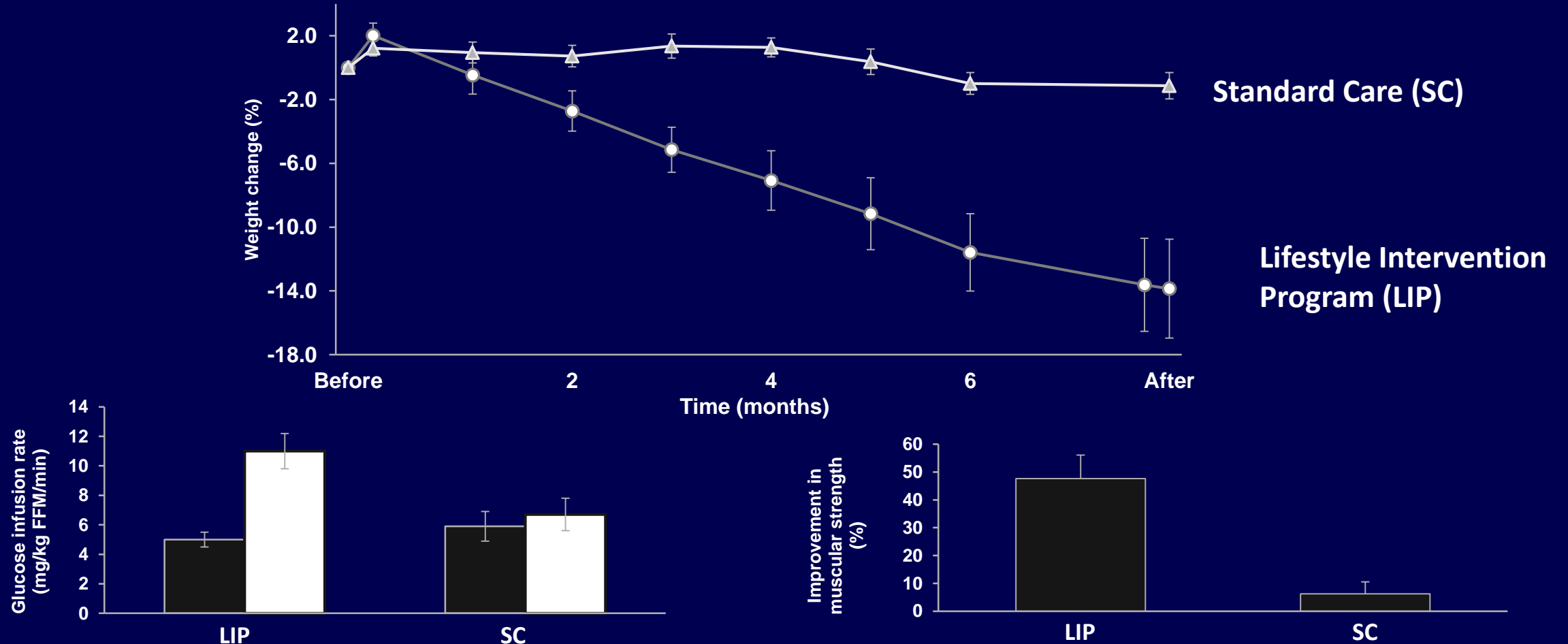
# Fatness, Fitness, and Cardiovascular Disease Mortality



Lee et al. *Am J Clin Nutr* 1999;69:373.



# Effect of Worksite Intensive Lifestyle Therapy in Employees with Type 2 Diabetes



Yoshino M et al. The Obesity Society 2015 Annual Meeting . Abstract T-P-LB-3790. November 2-6, 2016.

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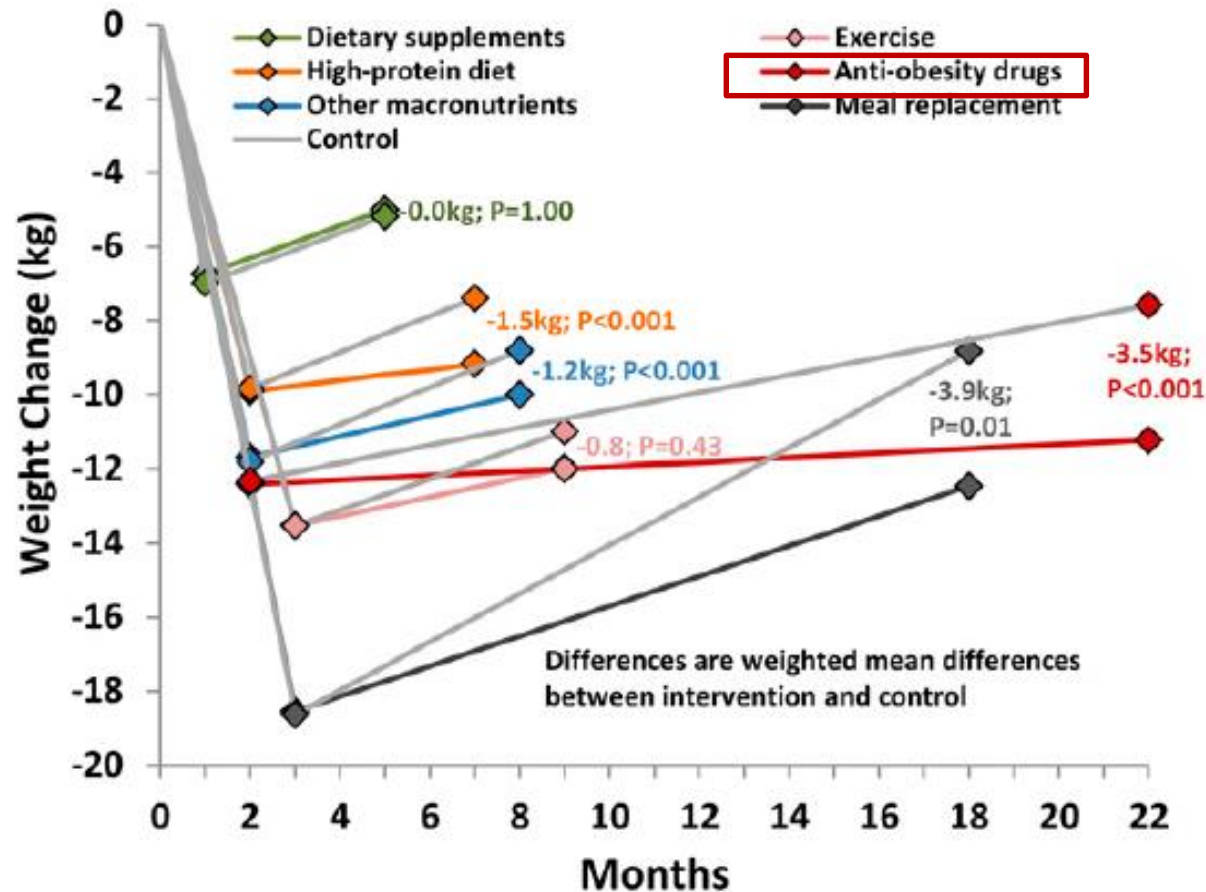
# Components of Behavior Therapy for Obesity



Wadden. *Med Clin North Am* 2000;84:441.

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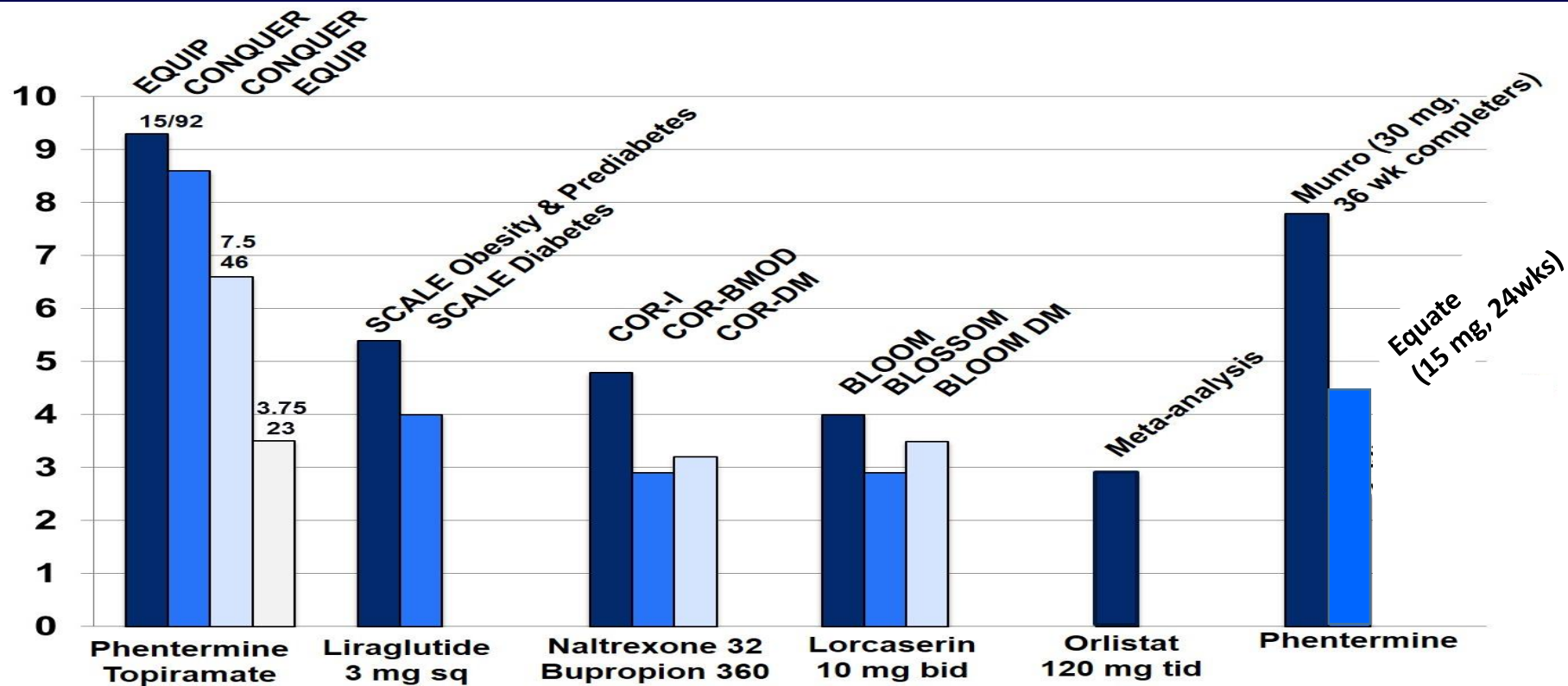
# Weight Loss Maintenance in 20 Randomized Controlled Trials



# FDA-Approved Drugs for Weight Loss

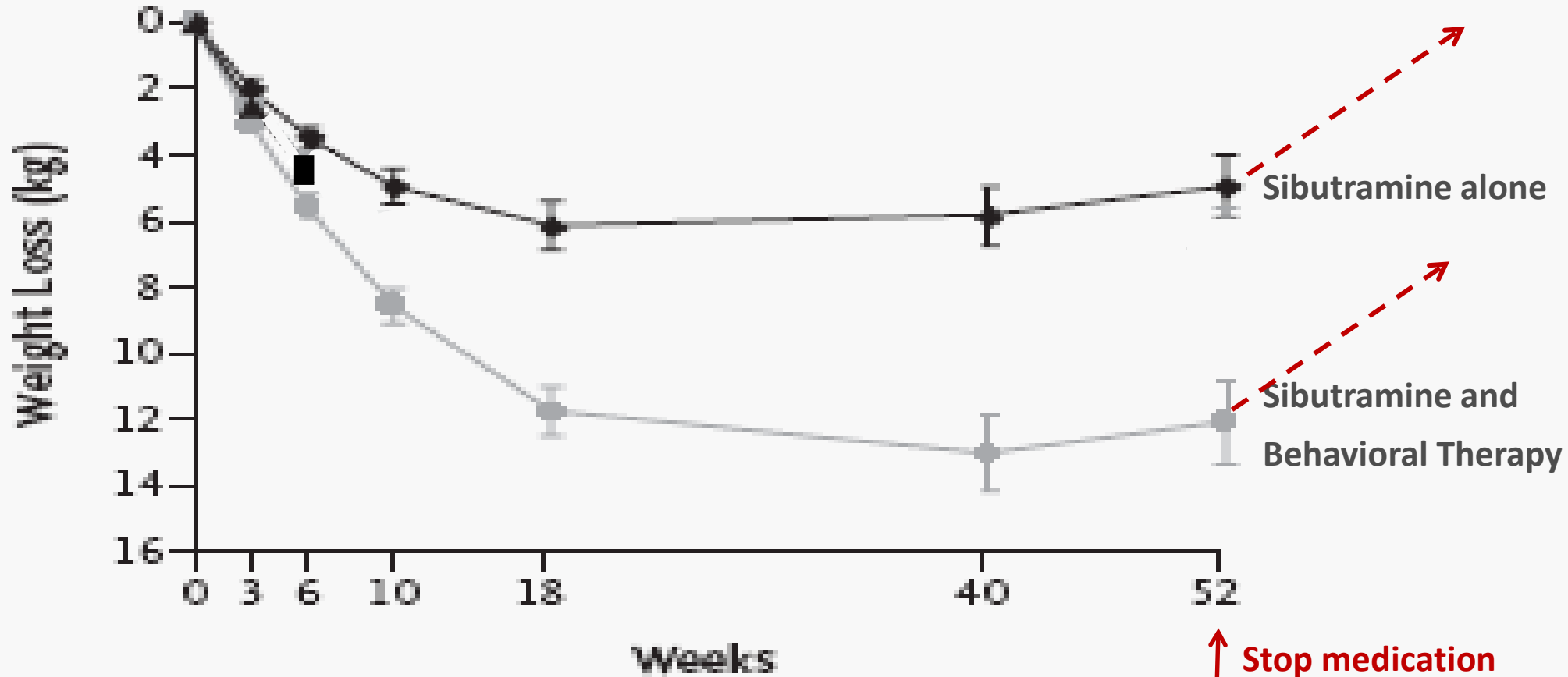
Year Approved	Generic Name
1947	Desoxyephedrine/methamphetamine
1956	Phenmetrazine
1959	Phentermine
1959	Diethylpropion
1959	Phendimetrazine
1960	Benzphetamine
1972	Fenfluramine Withdrawn 1997
1973	Mazindol
1996	Dexfenfluramine Withdrawn 1997
1997	Sibutramine Withdrawn 2010
1999	Orlistat
2012	Phentermine-Topiramate
2013	Lorcaserin
2014	Bupropion-Naltrexone
2015	Liraglutide

# Placebo-Subtracted Weight Loss of Obesity Medications (% weight loss at 1 year, ITT-LOCF)



Allison et al. *Obesity* (Silver Spring) (EQUIP). 2012;20:330–342; Gadde et al. *Lancet* (CONQUER). 2011;377:1341; Pi-Sunyer et al. *NEJM* (SCALE Obesity & Prediabetes). 2015;373:11-22; Davies et al. *JAMA* (SCALE Diabetes). 2015;314:687-699; Greenway et al. *Lancet* (COR-I). 2010 ;376:595-605; Wadden et al. *Obesity* (Silver Spring) (COR-BMOD). 2011;19:110-20; Hollander et al. *Diabetes Care* (COR-DM). 2013;36:4022-4029; Smith et al. *N Engl J Med* (BLOOM). 2010; 363:245-256; O'Neil et al. *Obesity* (Silver Spring) (BLOOM DM). 2012;20:1426-36; Fiddler et al. *J Clin Endocrinol Metab* (BLOSSOM). 2011;96:3067-77; Padwal et al. *BMJ* 2007;1194-9; Munro et al. *Br Med J*. 1968;1:352-4; Aronne et al. *Obesity* (EQUATE). 2013;21:2163-71.

# Additive Effects of Behavioral Therapy with Pharmacotherapy for Obesity



\*Sibutramine withdrawn from market.

Wadden et al. *N Engl J Med* 2005;353:2111.

# Treatment-oriented Classification of HyperBMlema



**Obesity-related risk factor:** Triglyceride/HDL-C  
Blood pressure  
IFG, IGT, HbA1c 6-6.5%  
Metabolic syndrome  
Family history (cancer, diabetes, CV disease)

**Obesity-related disease:** Diabetes  
Hypertension  
Dyslipidemia  
NAFLD: NAFL, NASH  
Pulmonary dysfunction: OSA, OHS  
Cardiovascular disease  
Osteoarthritis  
Infertility  
Urinary stress incontinence

**Obesity-related symptom/functional impairment:**  
Joint pain  
Impaired mobility/endurance  
Impaired quality-of-life