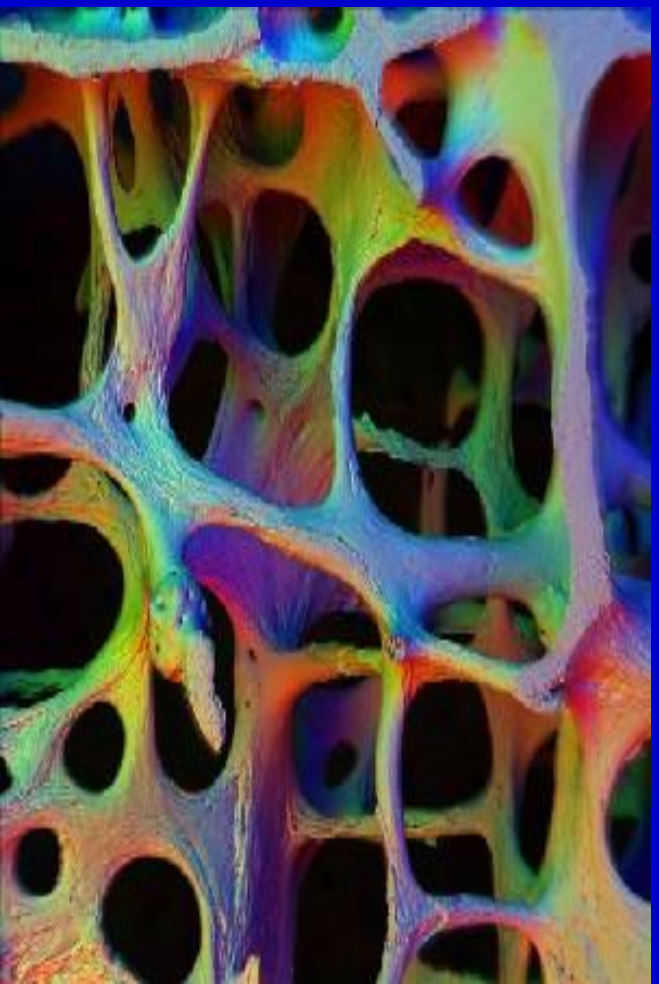
Bone and lifestyle intervention



Nicola Napoli, MD PhD
Div of Endocrinology
Campus Bio-Medico di Roma
Div Of Bone and Mineral Diseases
Washington University in St Louis

Washington University in St.Louis
School of Medicine

Background

- Lifestyle intervention (weight loss and exercise) is recommended as the cornerstone of obesity treatment at all ages.
- However, this recommendation remains controversial in obese older adults:

➢ exacerbation of age related lean tissue losses (sarcopenia)

➢ Feasibility of long-term weight loss

- There is little evidence from clinical trials regarding the benefits and risks of weight-loss interventions to guide the care of this population

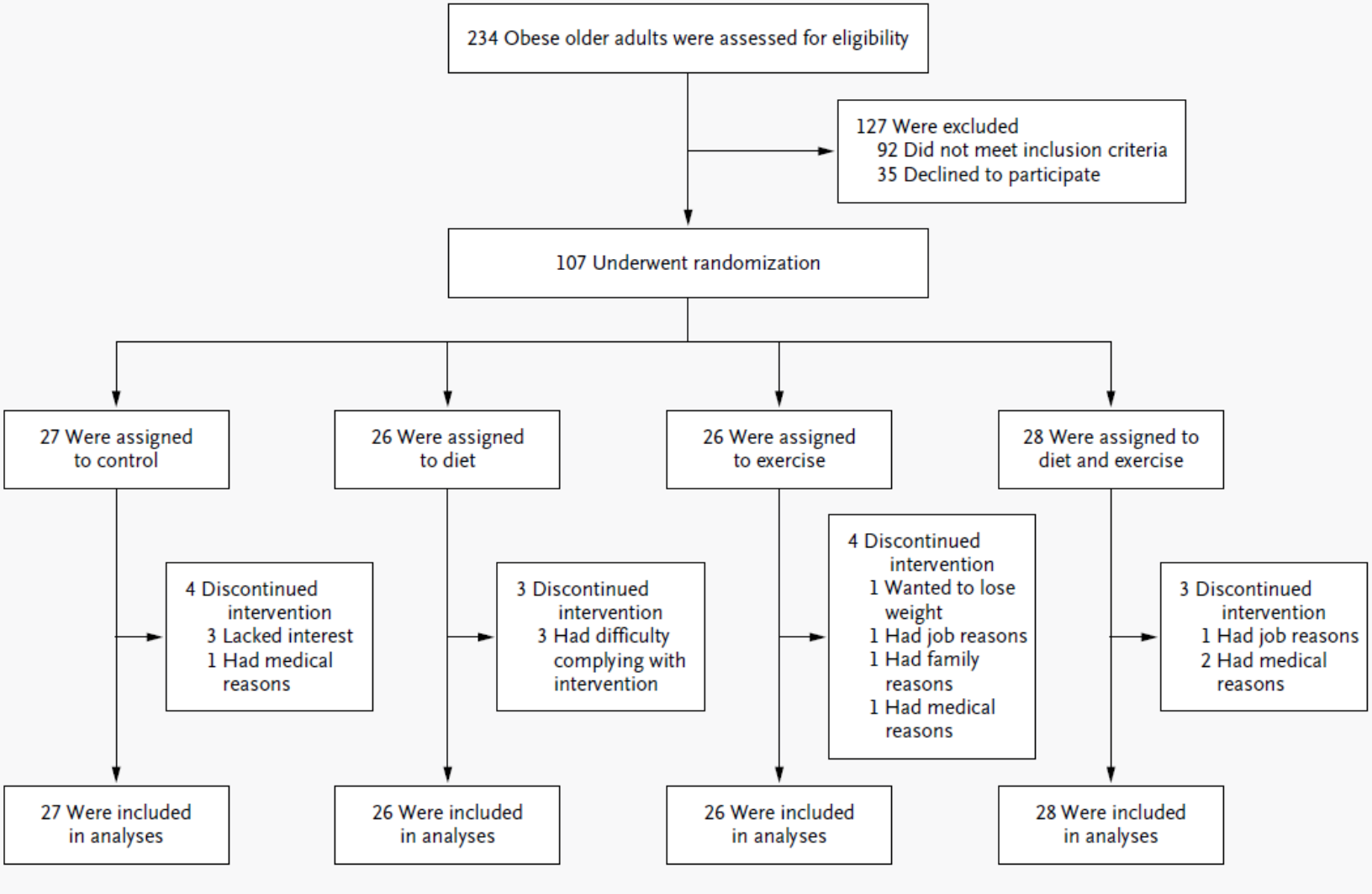


Figure 1. Screening, Randomization, and Follow-up.

Villareal, Napoli et al, NEJM 2011

Hypothesis

- weight loss and exercise would each improve physical function and that the combination of the two would result in the greatest improvement in physical function and amelioration of physical frailty.

EXERCISE

- **Group Exercise-Training Sessions**
- 3 nonconsecutive days a week
- Supervised by a physical therapist
- 15-min flexibility
- 30-min endurance (~80% of VO2peak)
- 30-min resistance (~80% of 1-RM)
- 15-min balance

Diet

- **Balanced Diet**
- Provide energy deficit of ~750 kcal/day
- Goal of 10% weight loss
- **Weekly Group Behavioral Therapy**
- Goal setting
- Self-monitoring
- Stimulus control
- Problem solving skills

Subjects

- BMI ≥ 30 kg/m2, age ≥ 65 yrs
- Sedentary, stable weight, stable medications
- Excluded
- severe cardiopulmonary disease
- musculoskeletal/neuromuscular impairments
- sensory or cognitive deficits
- history of malignancy
- steroid, androgen, and estrogen use

Evidence of Physical Frailty

- Two of the following operational criteria
- □ Physical Performance Test of 18 to 32
- □ VO2peak of 11 to 18 L/min/kg
- □ Difficulty or need for assistance in 1 basic or 2 instrumental ADL

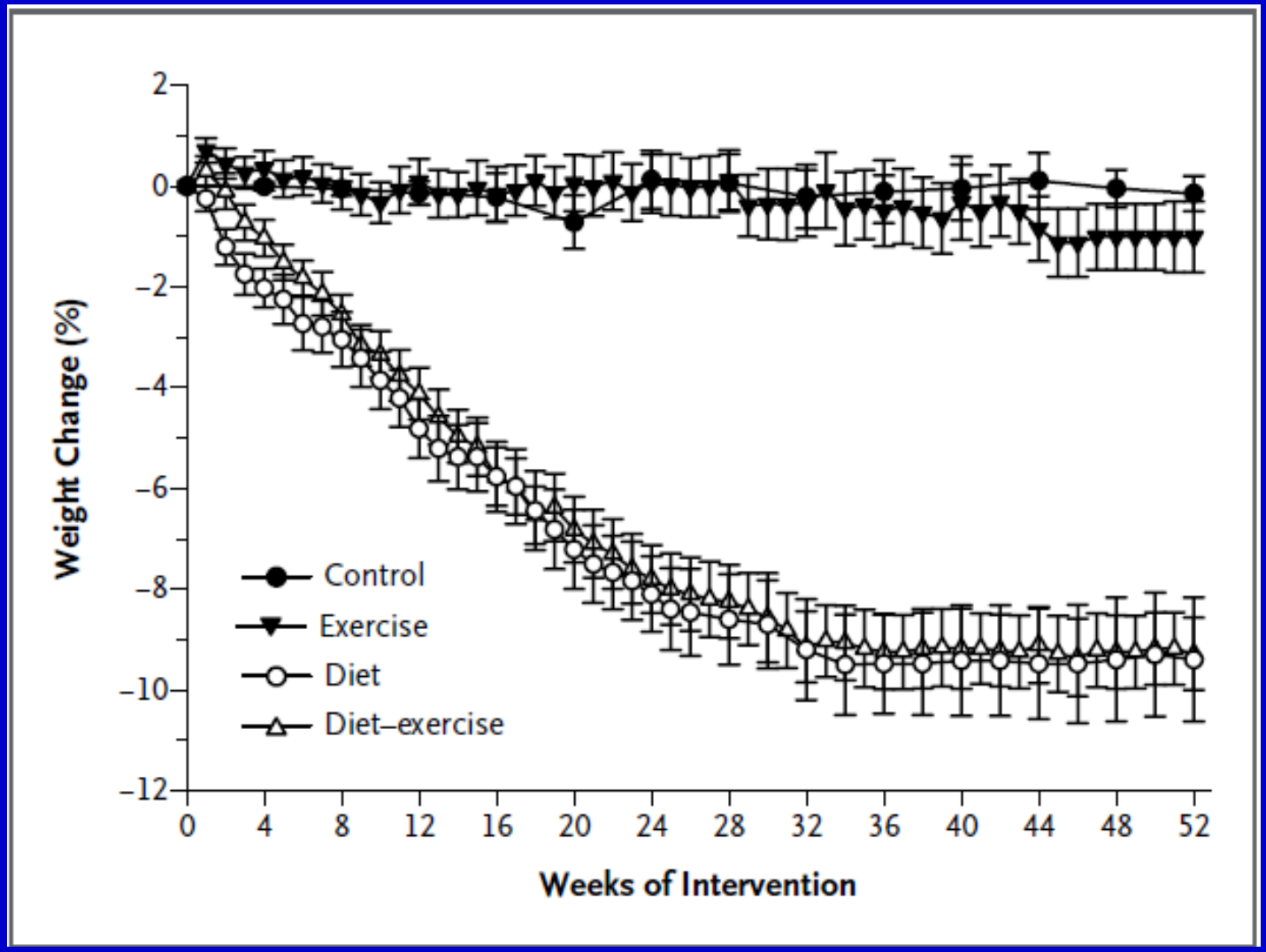
Results

Baseline clinical characteristics

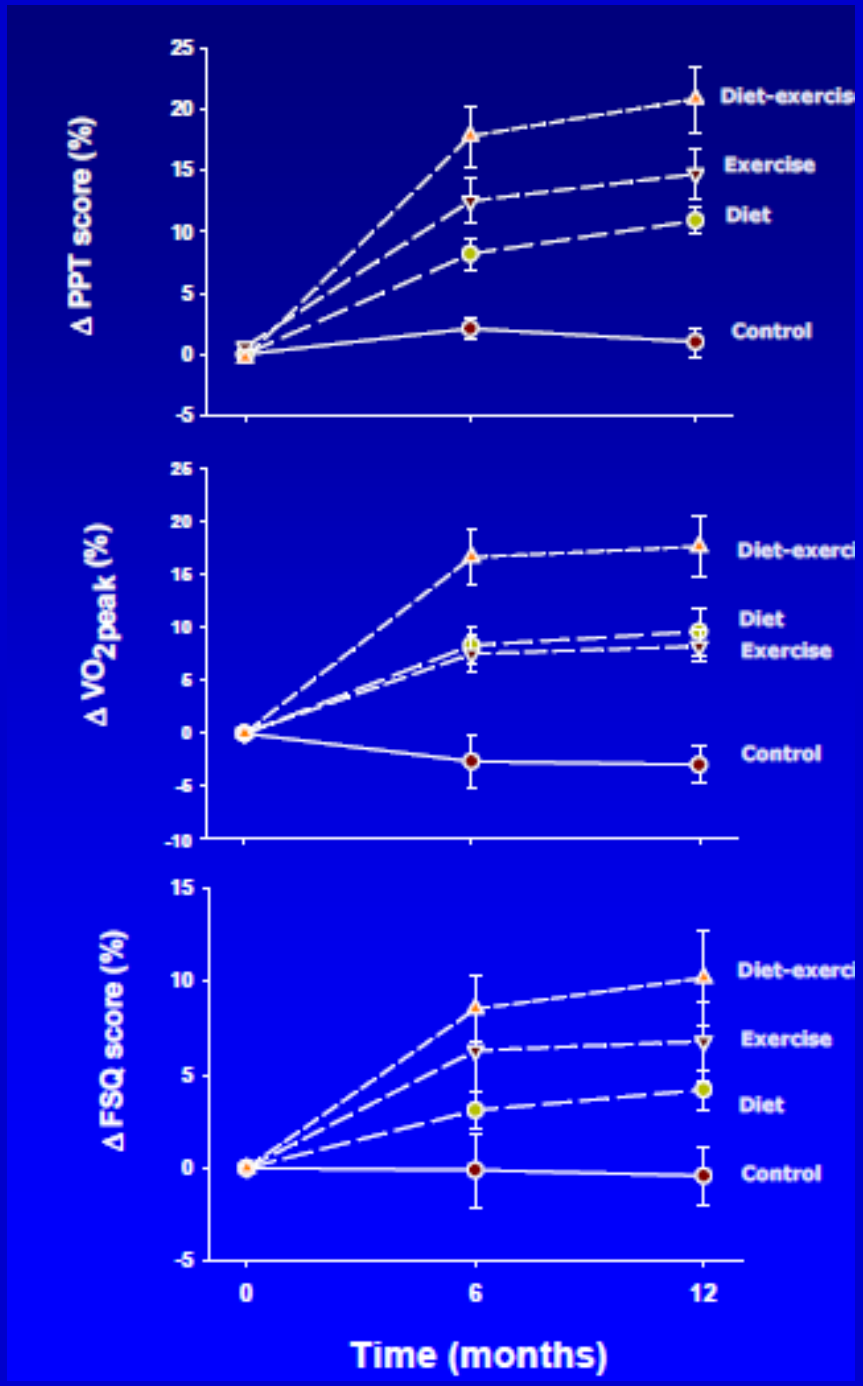
	CTRL (n=27)	Diet (n=26)	EX (n=26)	Diet-EX (n=28)	P value
Age (yr)	69±4	70±4	70±4	70±4	0.85
Female sex, No. (%)	18 (67)	17 (65)	16 (61)	16 (57)	0.89
White race, No. (%)	22 (81)	23 (88)	21 (81)	25 (89)	0.78
Weight (kg)	101±16	104±15	99±17	99±17	0.66
BMI (kg/m^2)	37.3±4.7	37.2±4.5	36.9±5.4	37.2±5.4	0.93
BMD at total hip (g/cm^2)	0.962±0.132	1.021±0.139	0.958±0.151	1.014±0.151	0.25
T-score at total hip	-0.18±0.91	0.34±97	-0.25±1.1	0.18±1.1	0.07
Serum sclerostin (ng/ml)	1.51±0.42	1.50±0.33	1.14±0.23	1.57±0.39	0.54

Values are means ± SD. BMD, bone mineral density; BMI, = body mass index

% Change in body weight



Villareal..Napoli et al, NEJM, 2011

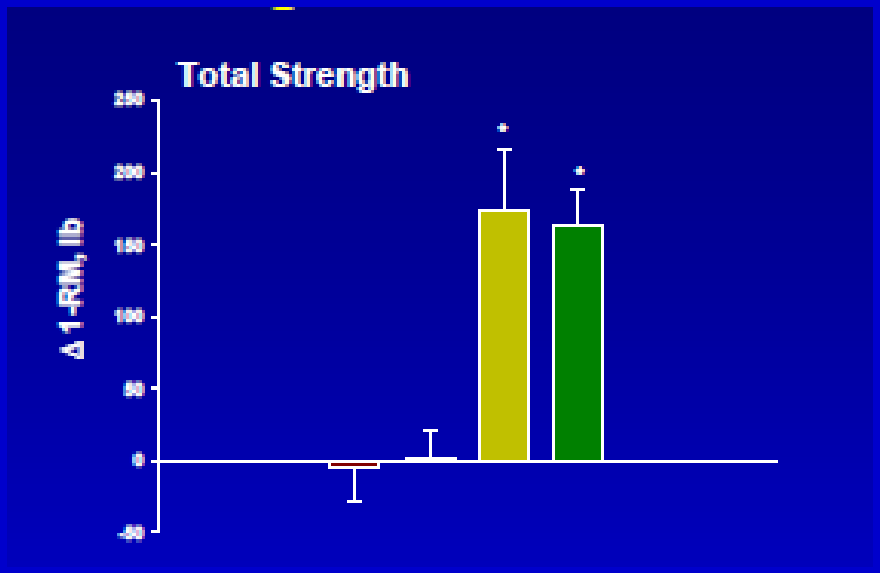


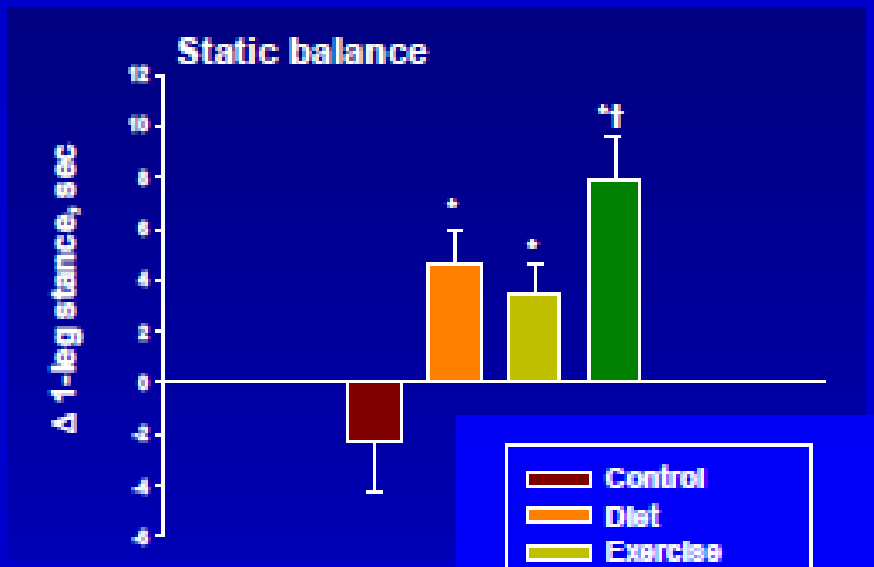
(PPT), which range from 0 to 36, with higher scores indicating better physical status (walking 50 ft, putting on and removing a coat, standing up from a chair, lifting a book, climbing one flight of stairs,

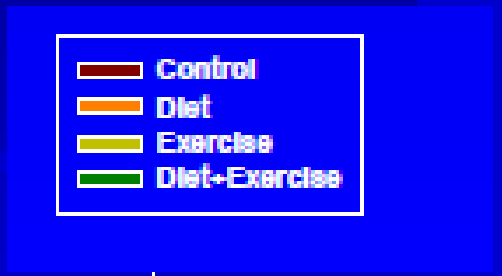
VO2 peak was assessed during graded treadmill walking

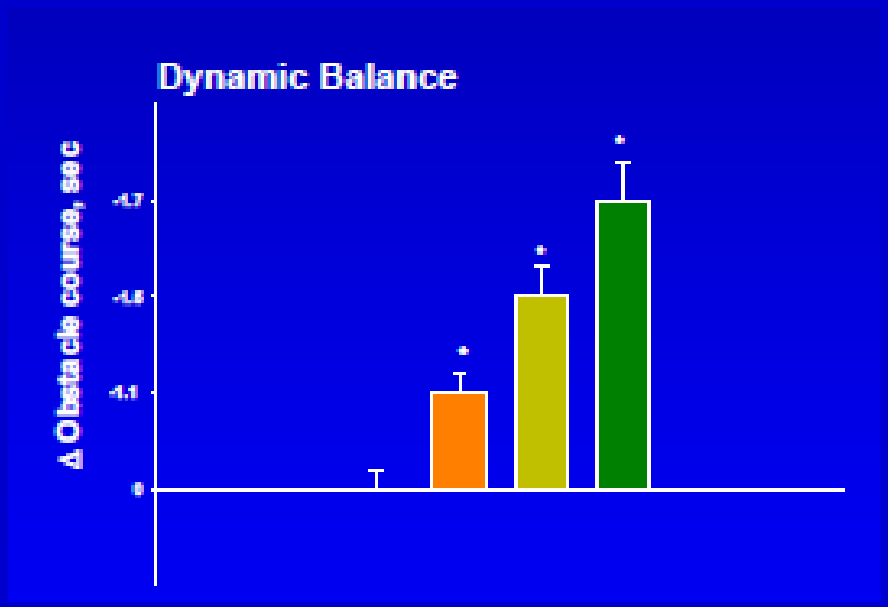
Functional Status Questionnaire (FSQ),
range from 0 to 36
activities of daily living
subjective measure of frailty

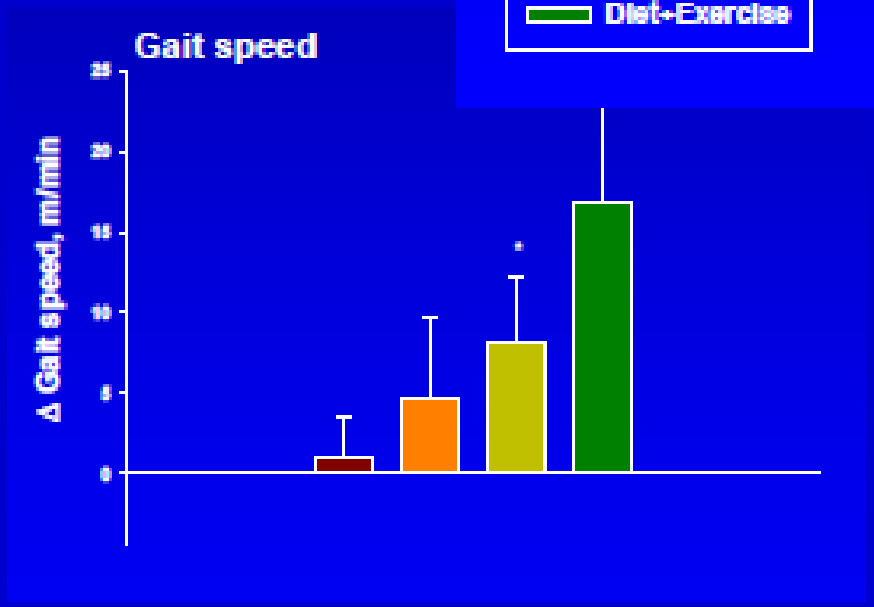
Effect of lifestyle intervrntion on Specific Physical Functions





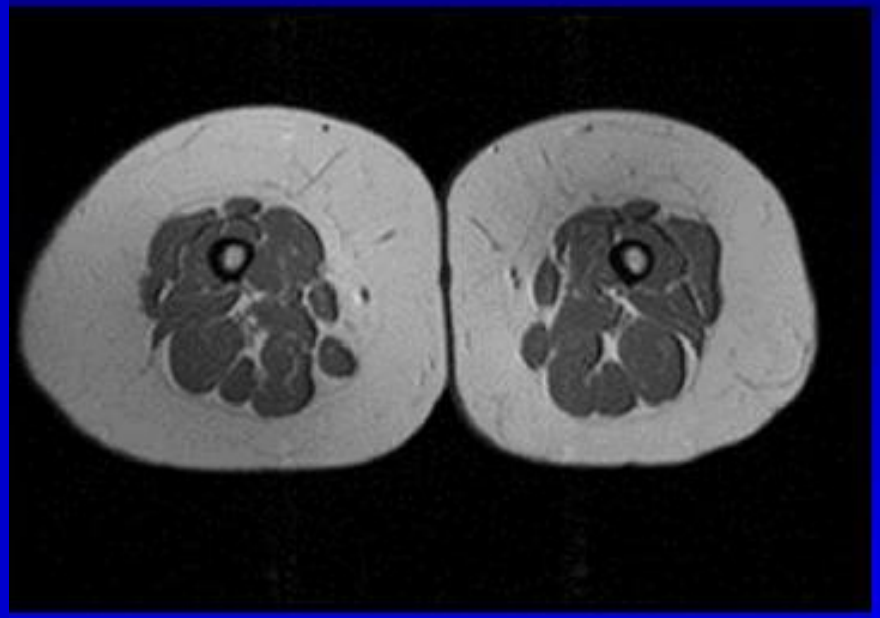






Weight Loss Therapy Improves Body Composition

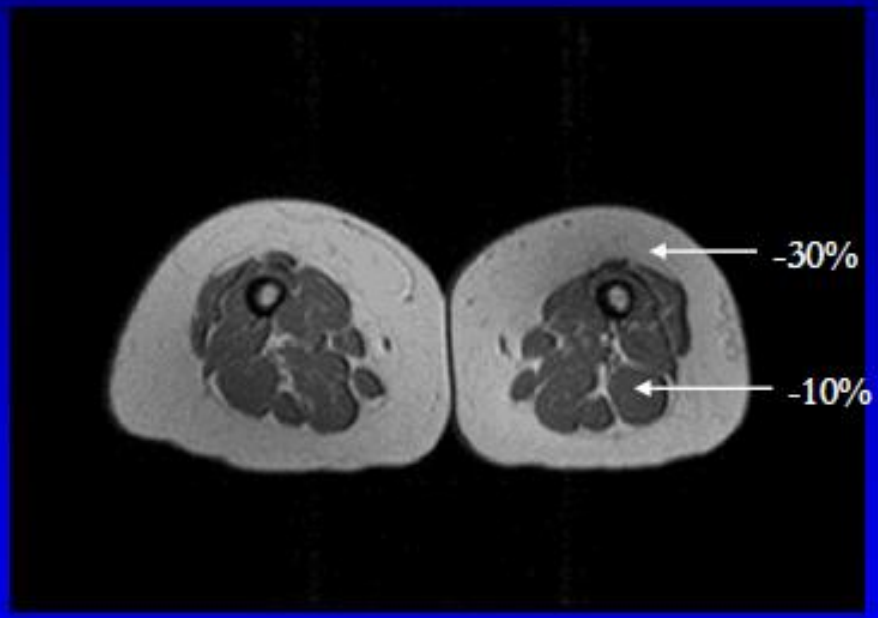
Before (Wt = 95 kg)



Fat = 48 kg
Lean = 47 kg
Relative Lean = 49%

PPT = 30 (Frail)

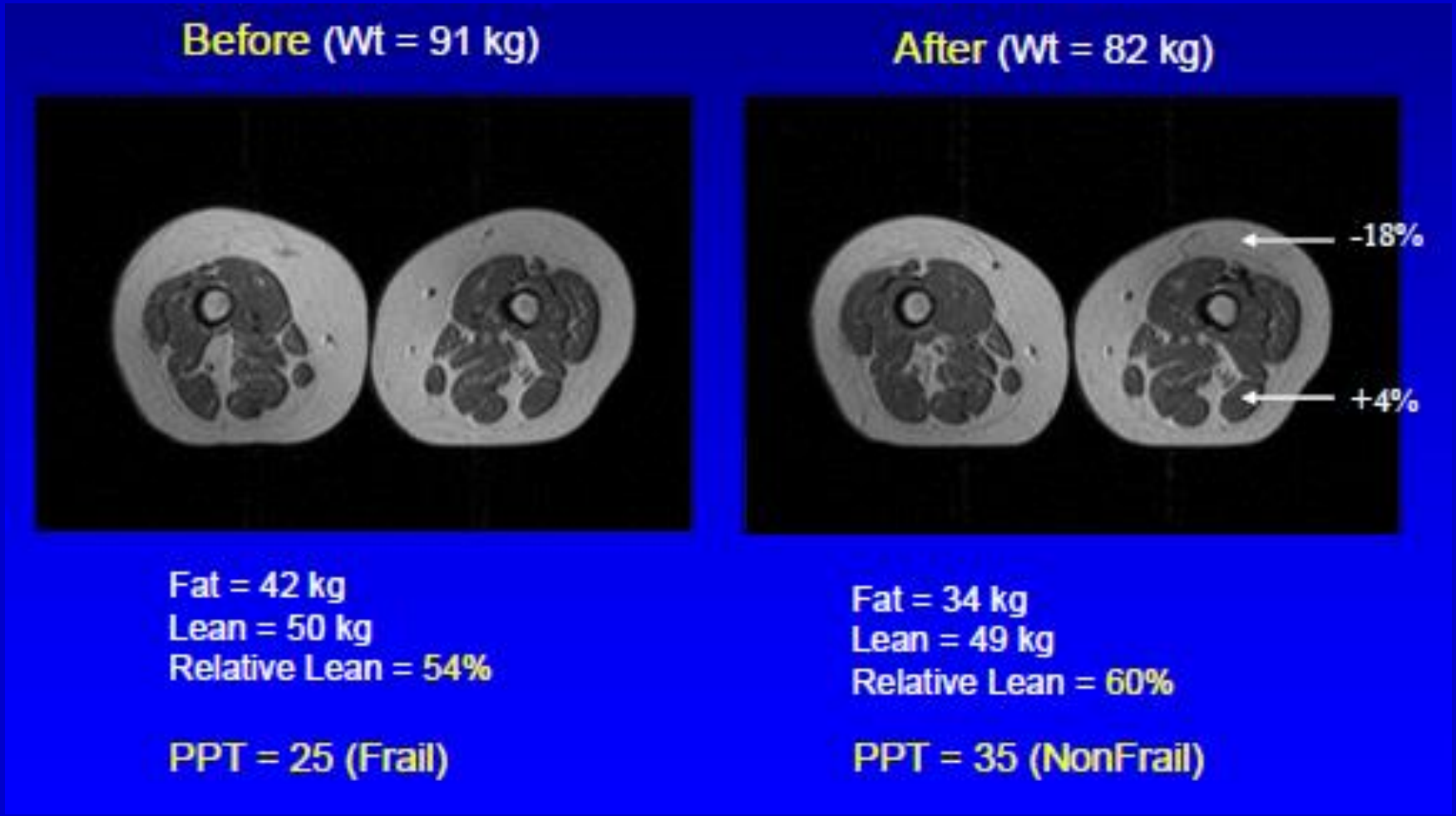
After (Wt = 75 kg)



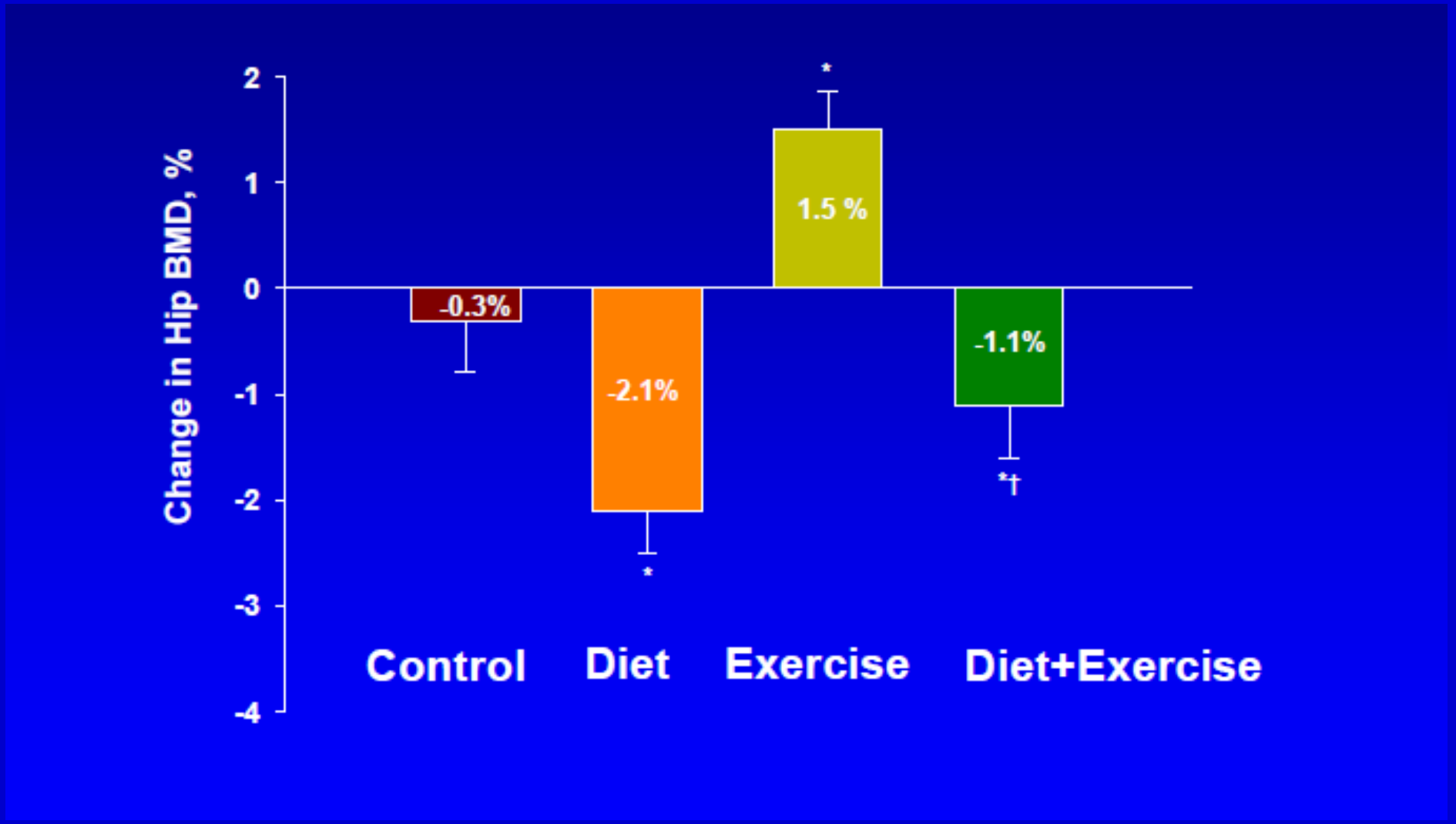
Fat = 33 kg
Lean = 42 kg
Relative Lean = 55%

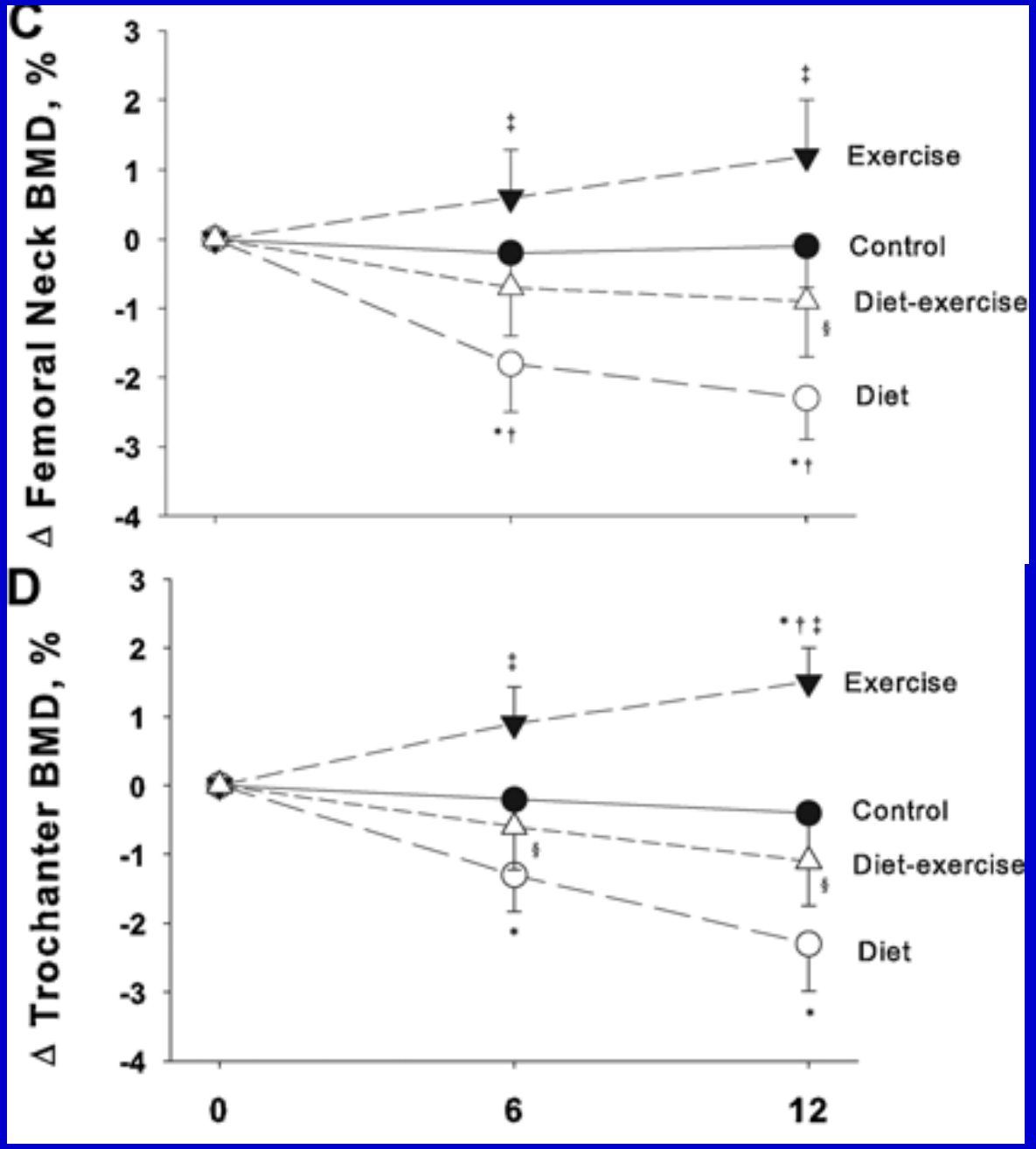
PPT = 35 (NonFrail)

Exercise added to Weight Loss Therapy Preserves Muscle Mass

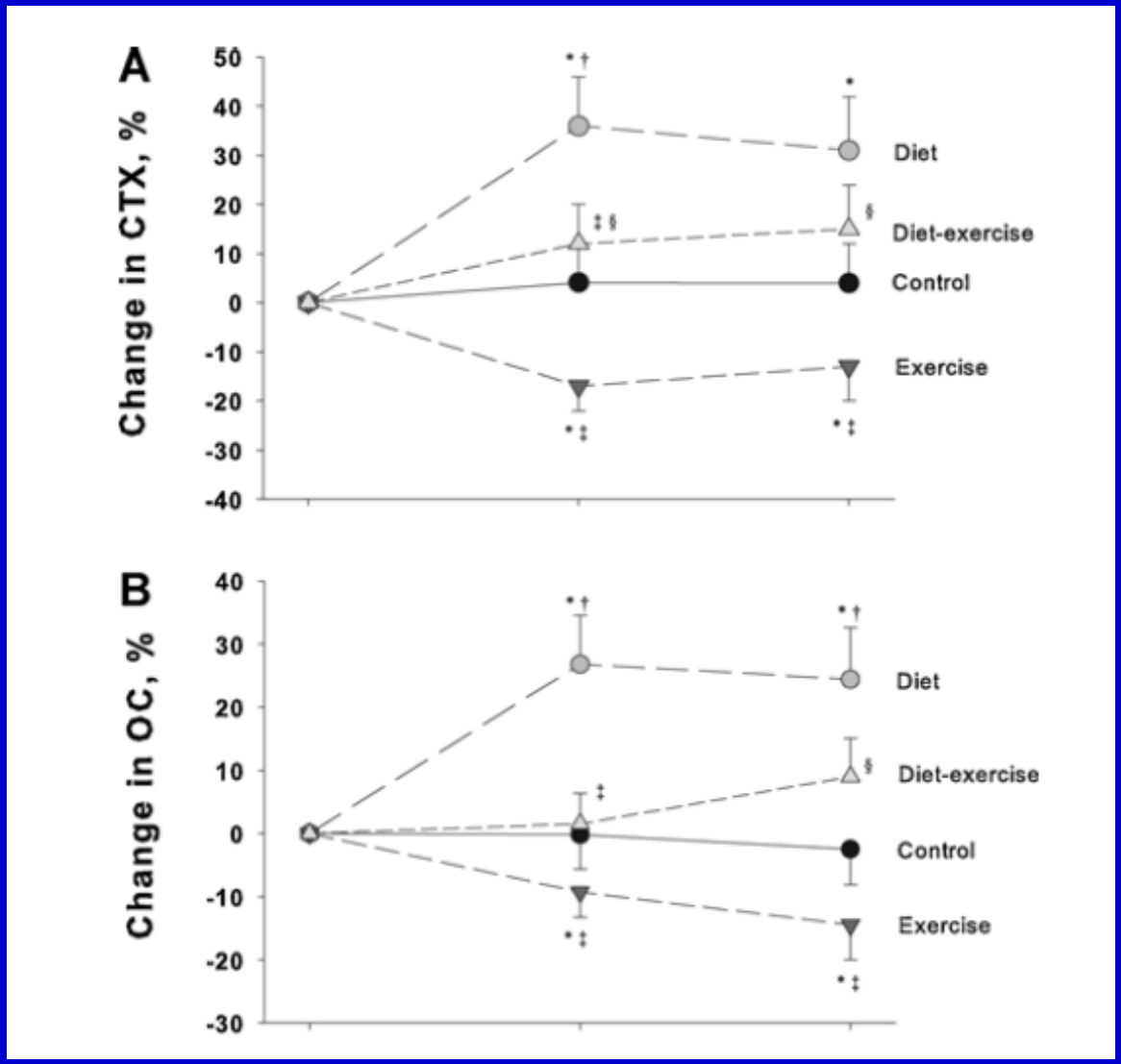


Changes from baseline in bone mineral density





Villareal..Napoli et al, NEJM, 2011



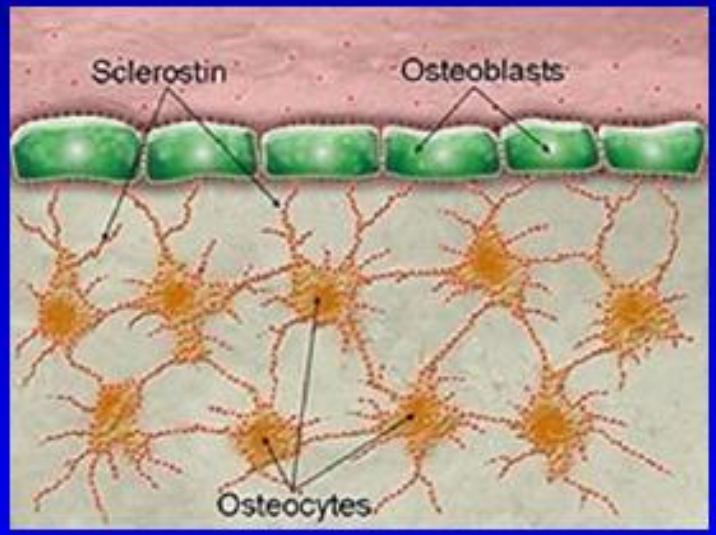
Villareal, Napoli et al, NEJM 2011

Summary

- the addition of exercise to weight-loss therapy among obese older adults prevents weight-loss-induced reduction in hip BMD and increase in bone turnover

Is sclerostin involved?

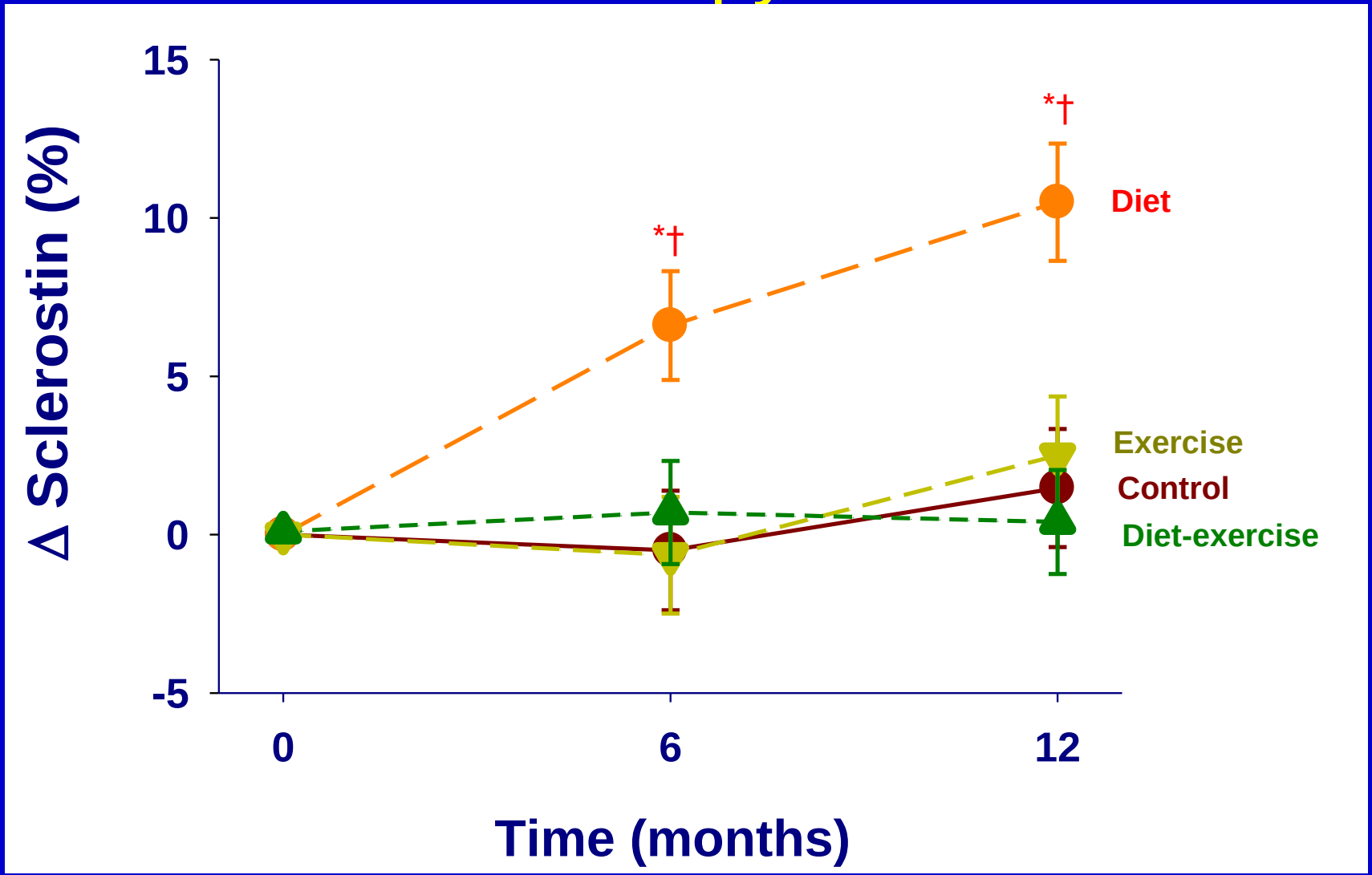
- Sclerostin is produced by osteocytes
  - ↓ bone formation
  - ↑ by unloading
- Loading ↓ sclerostin production



Hypothesis

- 1. That the effect of diet-induced weight loss and exercise (EX) on the skeleton is modulated by changes in SCL levels

Changes in Sclerostin with lifestyle therapy



Villareal, Napoli et al, JBMR 2012

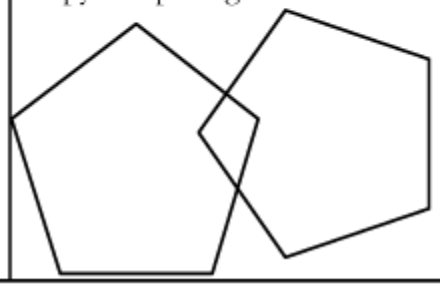
Memory and Obesity

- Obesity in older adults has been associated with both increased and decreased dementia risk
- Limited data from small, mostly short-term clinical trials suggest that weight loss and/or exercise may improve cognition, although other studies showed no effects
- Potential mediators of the effects of weight loss and/or exercise on cognition and quality of life still need to be elucidated

Cognitive Measures

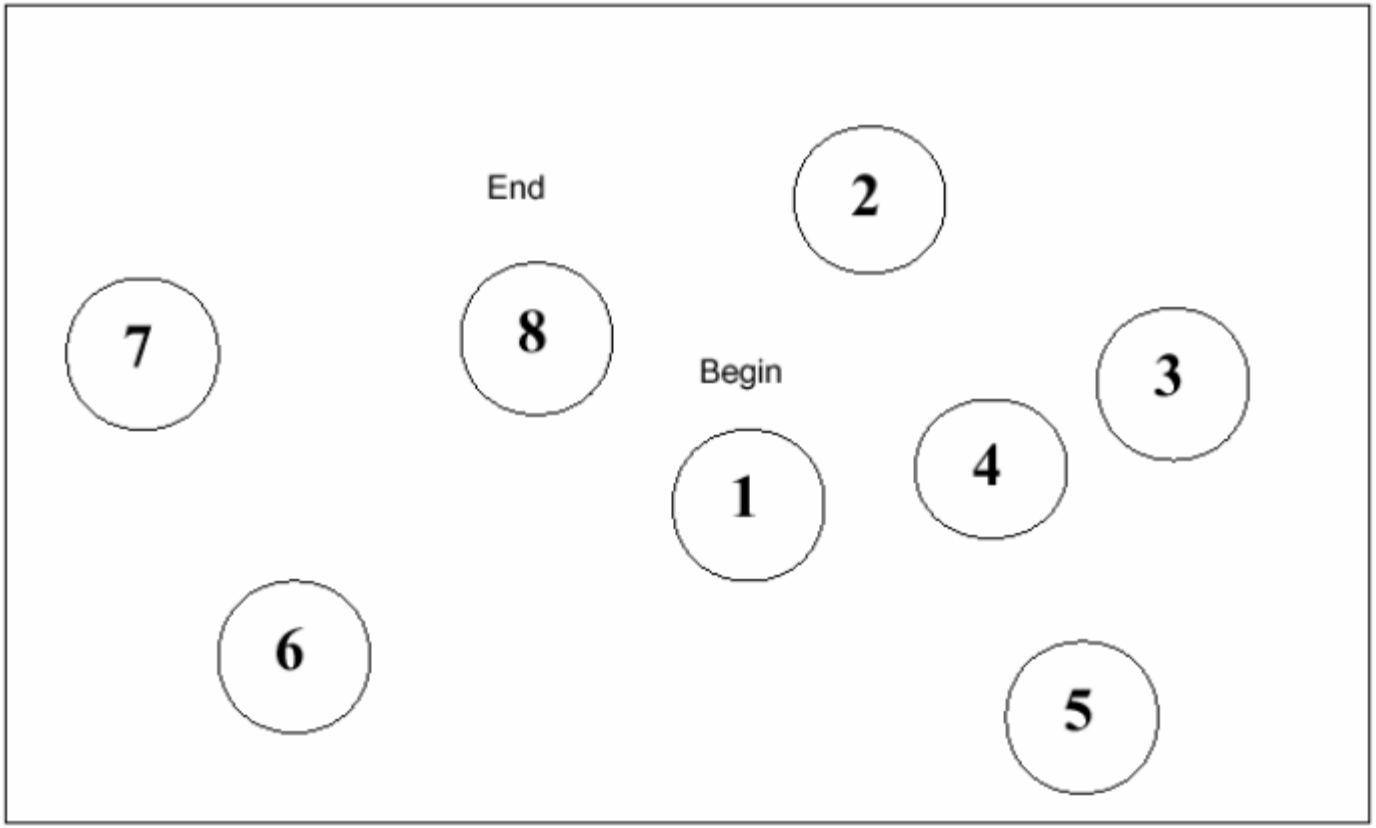
- GLOBAL COGNITION: Mini-Mental State Examination (score 1-100)
- VERBAL PRODUCTION, SEMANTIC MEMORY: Word List Fluency Test
- MENTAL FLEXIBILITY, AND EXECUTIVE FUNCTION: Trail Making Test Parts A and B
- MOOD: geriatric depression scale
- OBESITY-SPECIFIC QUALITY OF LIFE: IWQOL (1-100 scale)

Picture 1 – Mini mental state examination (MMSE)

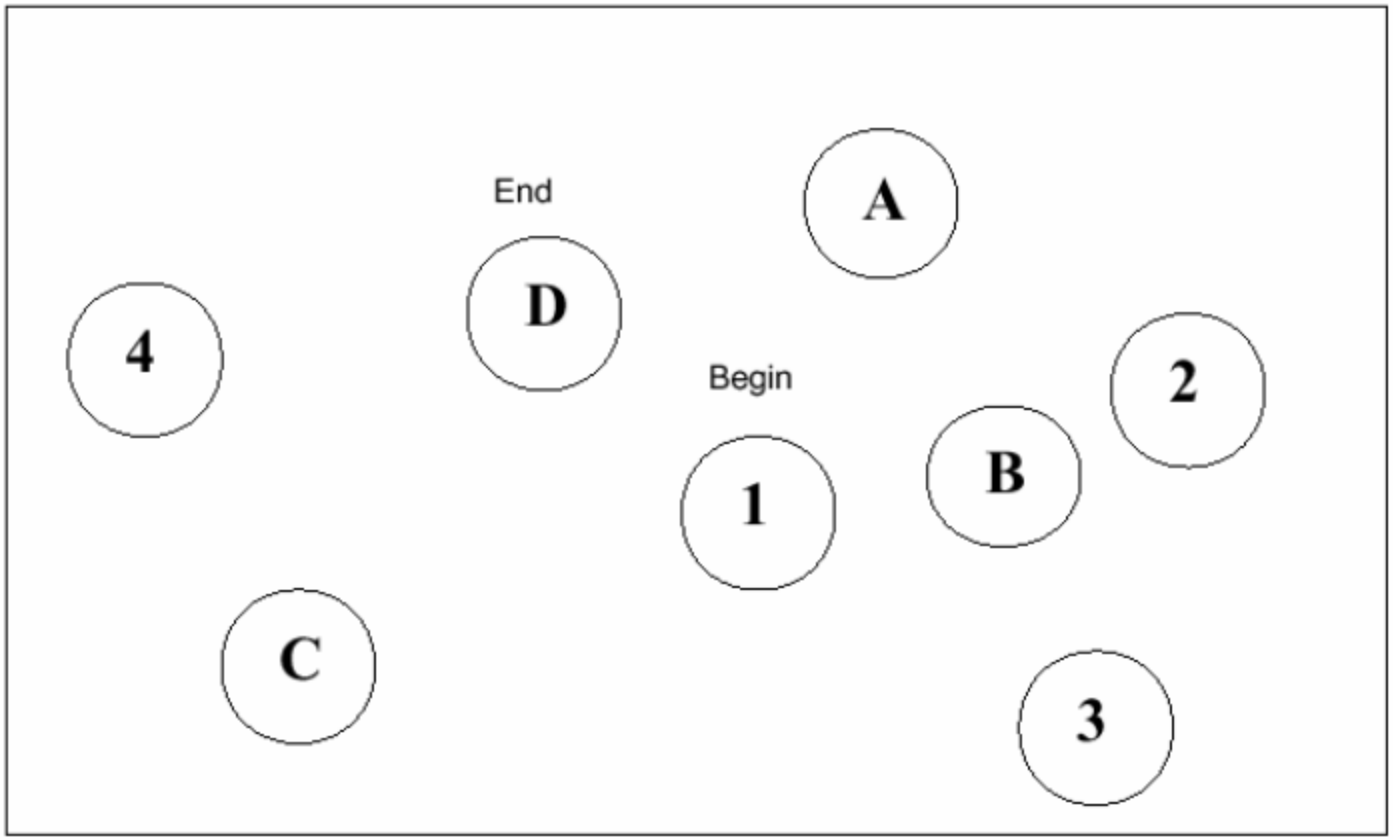
Temporal orientation (5 points)	What is the approximate time?
	What day of the week is it?
	What is the date today?
	What is the month?
	What is the year?
Spatial orientation (5 points)	Where are we now?
	What is this place?
	In what district are we or what is the address here?
	In which town are we?
	In which state are we?
Registration (3 points)	Repeat the following words: CAR, VASE, BRICK
Attention and calculation (5 points)	Subtract: 100-7 = 93-7 = 86-7 = 79-7 = 72-7 = 65
Remote memory (3 points)	Can you remember the 3 words you have just said?
Naming 2 objects (2 points)	Watch and pen
REPEAT (1 point)	"NO IFS, ANDS OR BUTS"
Stage command (3 points)	"Take this piece of paper with your right hand, fold it in half, and put it on the floor"
Writing a complete sentence (1 point)	Write a sentence that makes sense
Reading and obey (1 point)	Close your eyes
Copy the diagram (1 point)	Copy two pentagons with an intersection 

Fonte: Brucki SMD, Nitrini R, Caramelli P, Bertolucci PHF, Okamoto IH. Sugestões para o uso do mini-exame do estado mental no Brasil. Arq Neuropsiquiatr. 2003; 61(3B):777-81.

Trail Making Test Part A – *SAMPLE*

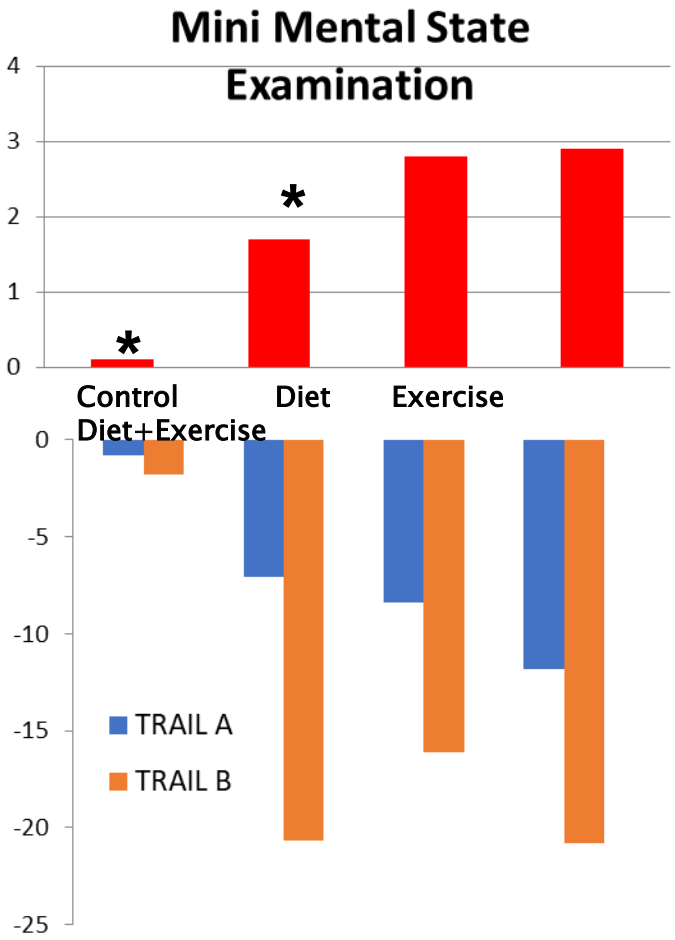


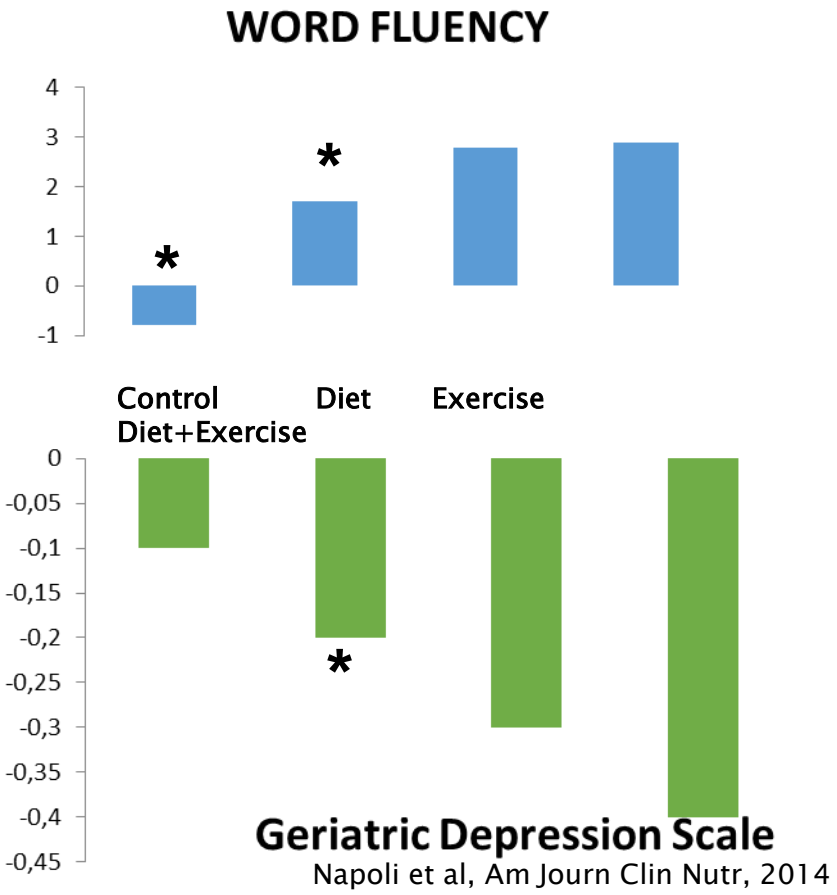
Trail Making Test Part B – *SAMPLE*



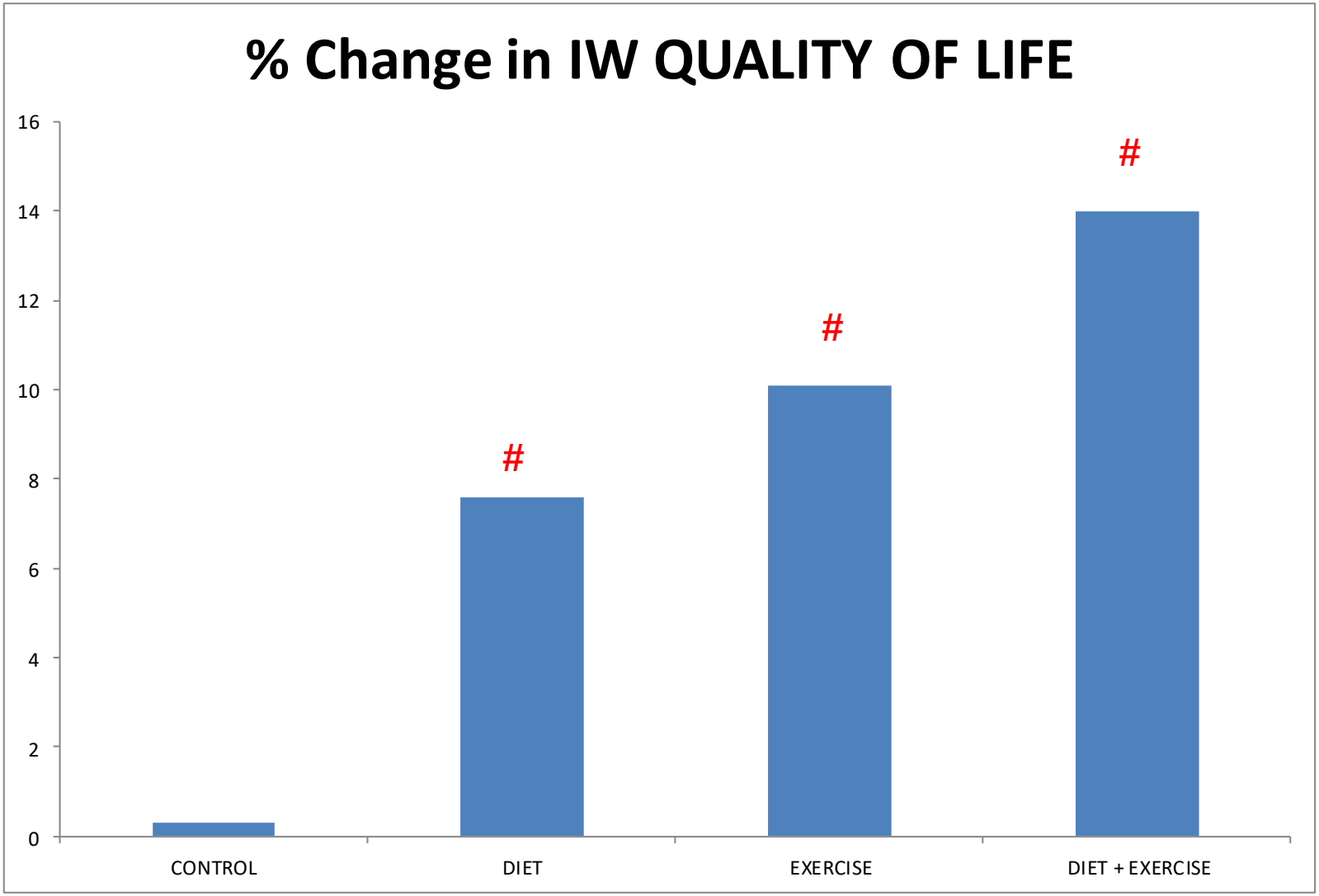
% Change from baseline for both cognitio

* p<0.005 vs. diet + exercise





Napoli et al, Am Journ Clin Nutr, 2014



Napoli et al, AJCN, 2014

Stepwise multiple linear regression analysis to identify which variables were independent contributors in each intervention group

Final model of variables affecting change in 3MS		
Diet group (multiple $R = 0.503$, $P = 0.0003$)		
Change in ISI	0.468 ± 0.119	0.0001
Change in hs-CRP	−0.309 ± 0.119	0.01
Exercise group (multiple $R = 0.489$, $P = 0.001$)		
Change in VO_{2peak}	0.319 ± 0.121	0.01
Change in LE 1-RM strength	0.314 ± 0.131	0.01
Diet-exercise group (multiple $R = 0.436$, $P = 0.002$)		
Change in LE 1-RM strength	0.272 ± 0.136	0.03
Change in VO_{2peak}	0.257 ± 0.124	0.04
Final model of variables affecting change in total IWQOL		
Diet group ($R = 0.383$, $P = 0.002$)		
Change in body weight	−0.383 ± 0.123	0.002
Exercise group strength ($R = 0.406$, $P = 0.002$)		
Change in LE 1-RM	0.406 ± 0.149	0.002
Diet-exercise group (multiple $R = 0.564$, $P = 0.0001$)		
Change in body weight	−0.365 ± 0.128	0.004
Change in LE 1-RM strength	0.293 ± 0.116	0.01

Napoli et al, AJCN, 2014

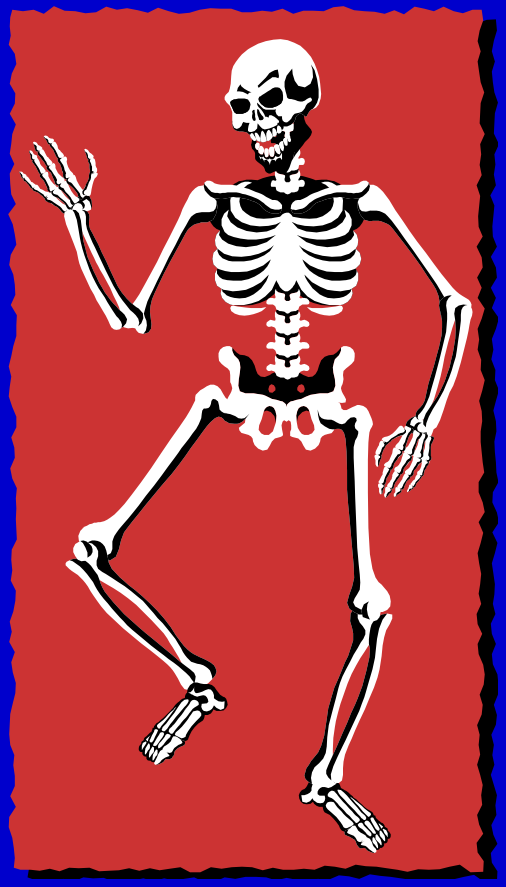
Summary

- Weight loss plus exercise and exercise alone equally improved scores in the global 3MS, TRAIL A and B tests and to a greater extent than weight loss alone
- Weight loss plus exercise and exercise alone equally improved scores in the IWQOL and to a greater extent than weight loss alone

Conclusions

- Successful weight loss (~10%) is feasible in frail, obese older adults.
- The addition of a exercise (multi-component) to weight-loss does not prevent but attenuates weight-loss-induced decrease in lean body mass.
- Weight loss alone and exercise alone improves physical function and ameliorates frailty in obese older adults.
- However, combined weight loss and regular exercise may provide greater improvement in physical function than either intervention alone.
- Weight loss therapy may decrease BMD (? clinical significance).
- Further studies are needed to determine whether weight loss can be maintained >1 year and prevent institutionalization of obese older adults.

GRAZIE



Support your bones.
They support you.