Contemporary Use of Meal Replacement Products for the Treatment of Obesity
VLCD and Beyond

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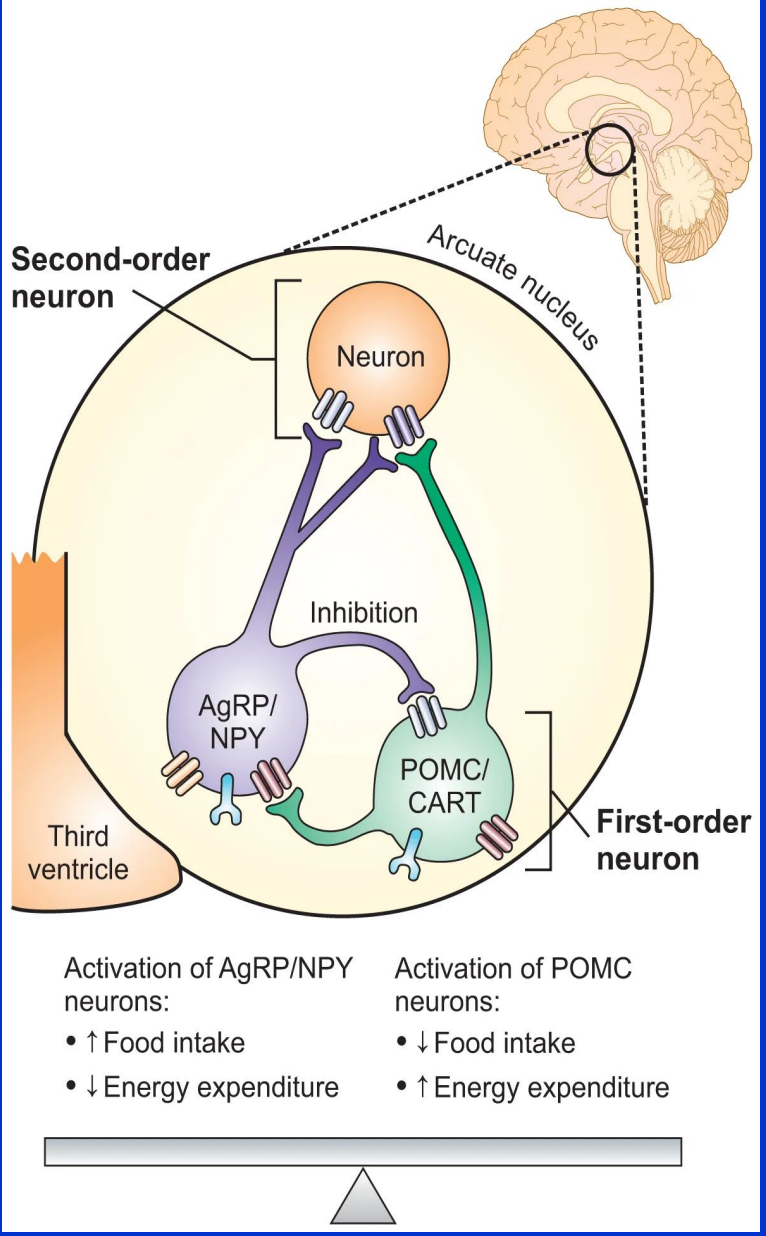
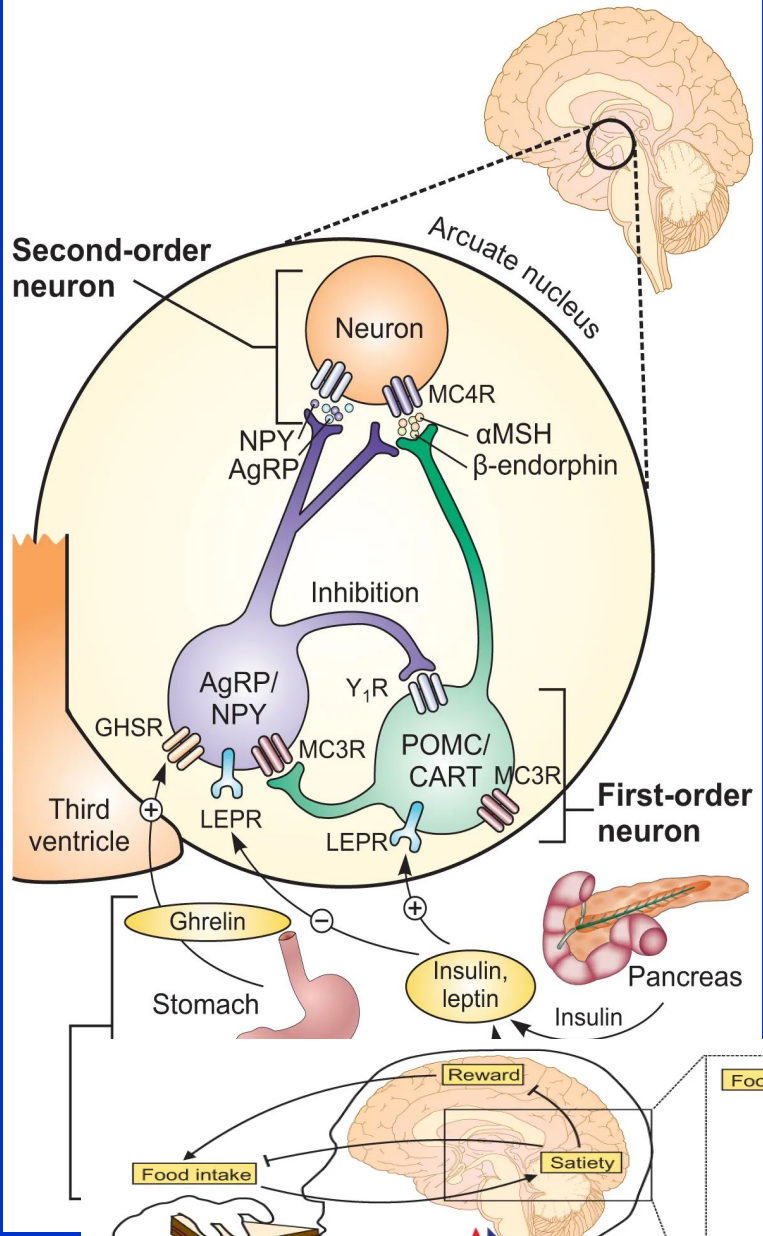
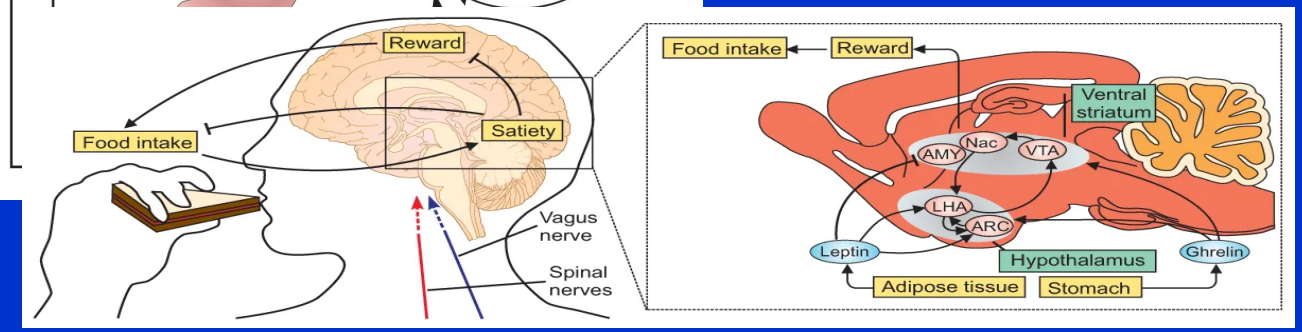
Objectives

- Review the foundation of obesity management
- Review the safety and efficacy of the VLCD in obesity management
- Review the role and effective use of meal replacement products in all aspects of obesity management

Science



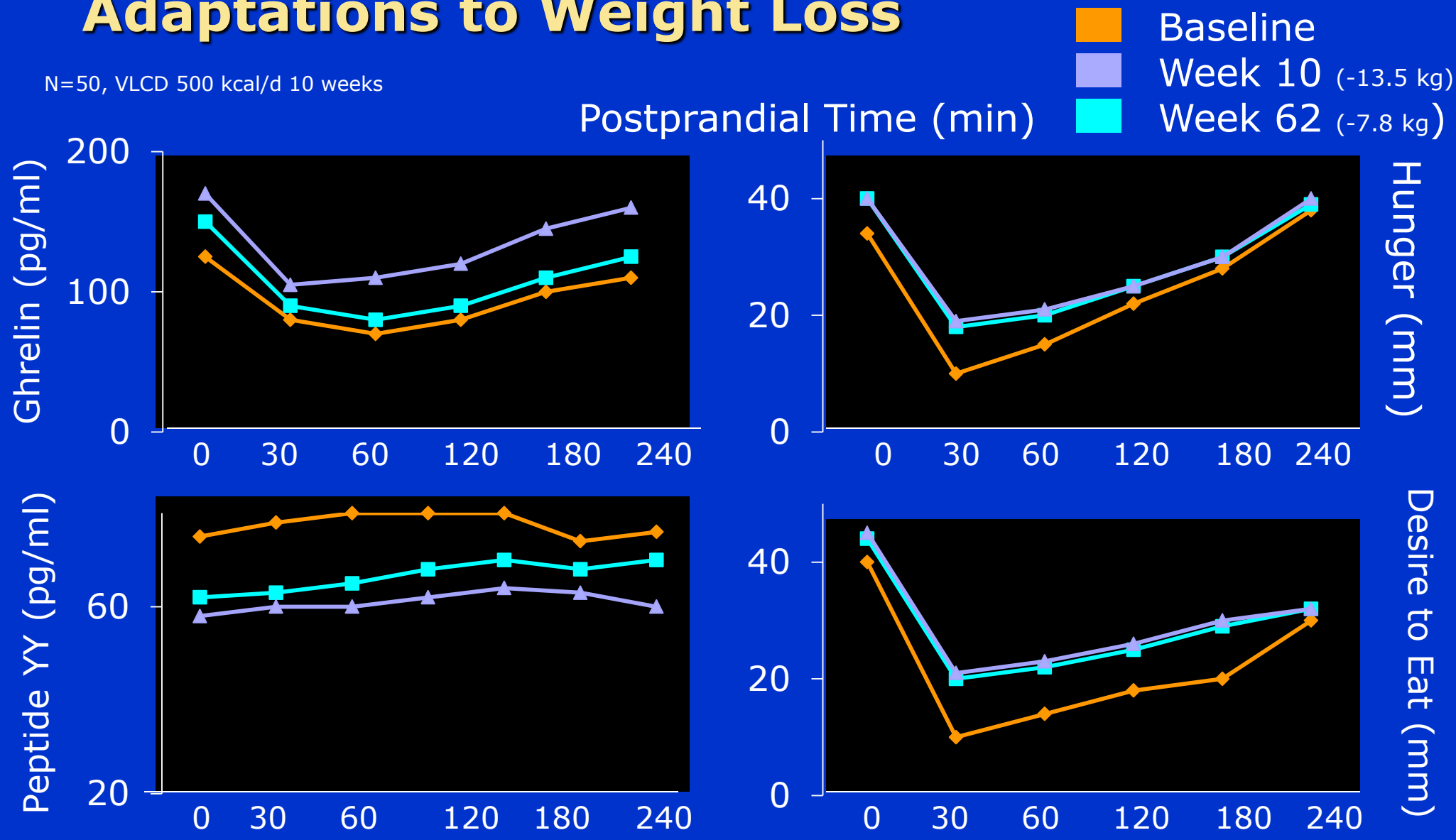




Modified from Vetter ML, et al. *Nat Rev Endocrinol*. 2010; 6:578-588; and Saper CB, et al. *Nature*. 2005;437(7063):1257-1263.

Long-Term Persistence of Hormonal Adaptations to Weight Loss

N=50, VLCD 500 kcal/d 10 weeks

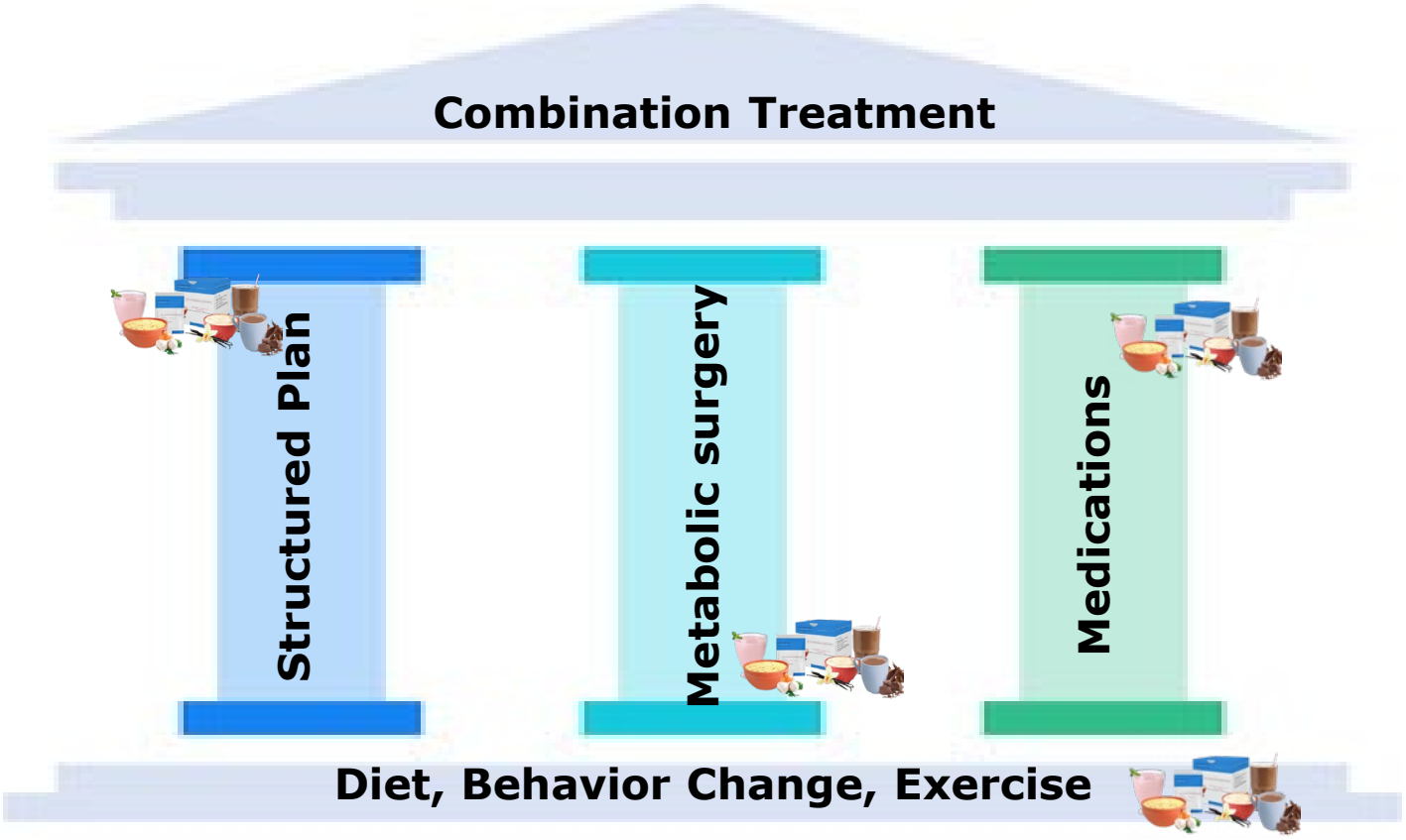


Sumithran et al. NEJM 2011;365:1597-604

- Complex physiological feedback mechanisms regulate bodyweight and resist weight loss. Slowing of metabolism can be substantial and persistent and plays a role in halting weight loss and putting subsequent weight regain into motion.
- However, the typical bodyweight trajectory is primarily driven by patients experiencing an exponential decay of diet adherence due to increase in appetite in proportion to the loss of bodyweight, along with difficulties in sustaining changes to dietary choices and behaviors that affect patients' ability to enjoy, celebrate, and socialize with food.

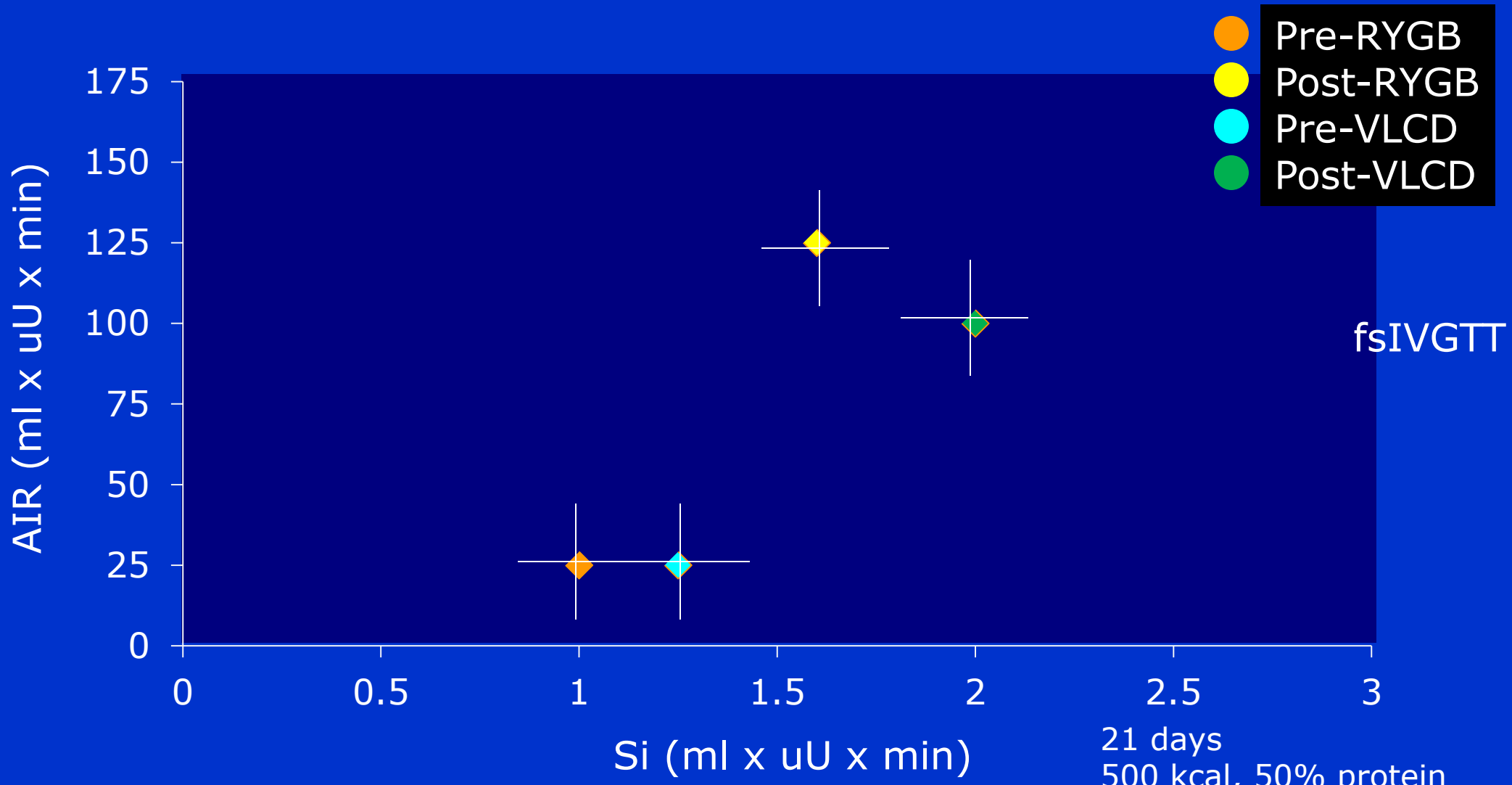
Polidori et al. Obesity (2016) 24, 2289-95

Coliseum of Weight Management



VLCD

Very Low Calorie Diet Mimics the Early Beneficial Effect of Roux-en-Y Gastric Bypass on Insulin Sensitivity and Beta-cell Function in Type 2 Diabetic Patients



21 days
500 kcal, 50% protein
Glucose, hormones similar

Diabetes 2013. Jackness et al. (62) 3027-32

Effect of Diet versus Gastric Bypass on Metabolic Function in Diabetes

- n= 22
- 18% weight loss
- Weight loss was associated with increases in suppression of glucose, increases in insulin-stimulated glucose disposal and increased beta-cell function.
- No differences between groups

Yoshino et al. NEJM 2020;383:721-32.

Very Low Calorie Diets

- 800 kcal/diet (600-1000 kcal)
- 2-5lb + weekly weight loss
- Meal replacements
- Quality protein/electrolytes
- Medical supervision/comprehensive/multidisciplinary
- USPTF
- Relative contraindications
- Transition to LCD

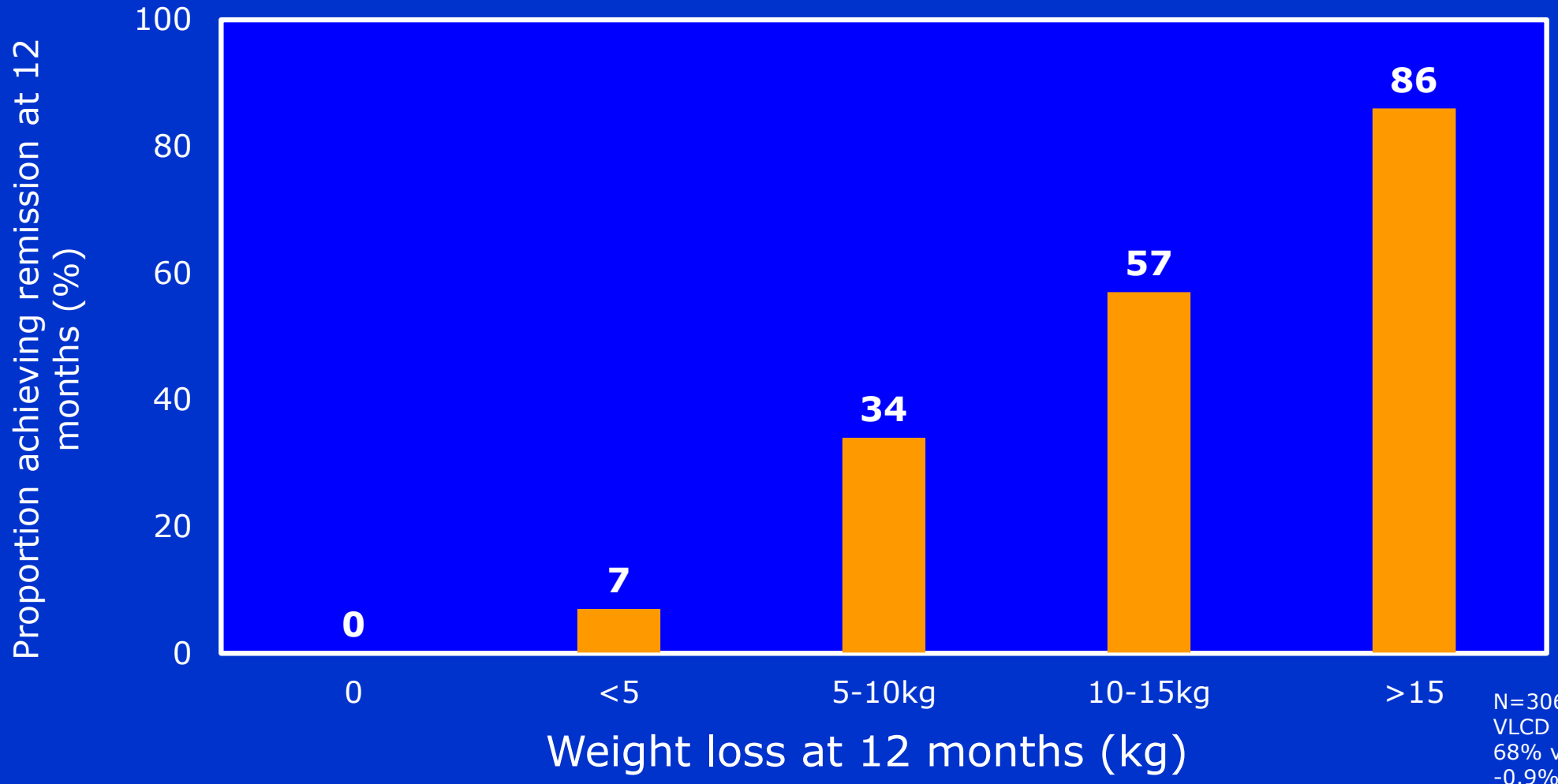
Obesity Management Guidelines
VLCD

- USPTF – intensive, multicomponent behavioral interventions in adults with obesity can lead to significant improvements in weight
- AACE – VLCD can lead to diabetes remission and > 10% weight loss can ameliorate obesity related diseases
- AHA/TOS – advise > 6 months in comprehensive program, VLCD with medical monitoring

JAMA. 2018;320(11):1163-71
Endocrine Practice. 28 (2022) 923-1049.
Circulation. 2014;129: S102-138

Primary care-led weight management for remission of type 2 diabetes (DIRECT): an open-label, cluster randomized trial

Local staff/ 8h



N=306
VLCD 800 kcal
68% vs 4%
-0.9% A1c vs +0.1
10 kg vs 1 kg loss
+ QOL

Lean et al. *Lancet*. Feb 10,2018

Clinical effectiveness of very-low-energy diets in the management of weight loss: a systematic review and meta-analysis of randomized controlled trials

- Compared with a behavior program alone, VLEDs combined with a behavior program achieved -3.9 kg at 1 year. The difference at 24 months -1.4 kg and -1.3 kg at 36-60 months
- 19% drop out VLED vs 20% comparator
- "Very-low energy diets with behavioural programmes achieve greater long-term weight loss than behavioural programmes alone, appear tolerable and lead to few adverse events suggesting they could be more widely used than current guidelines suggest.

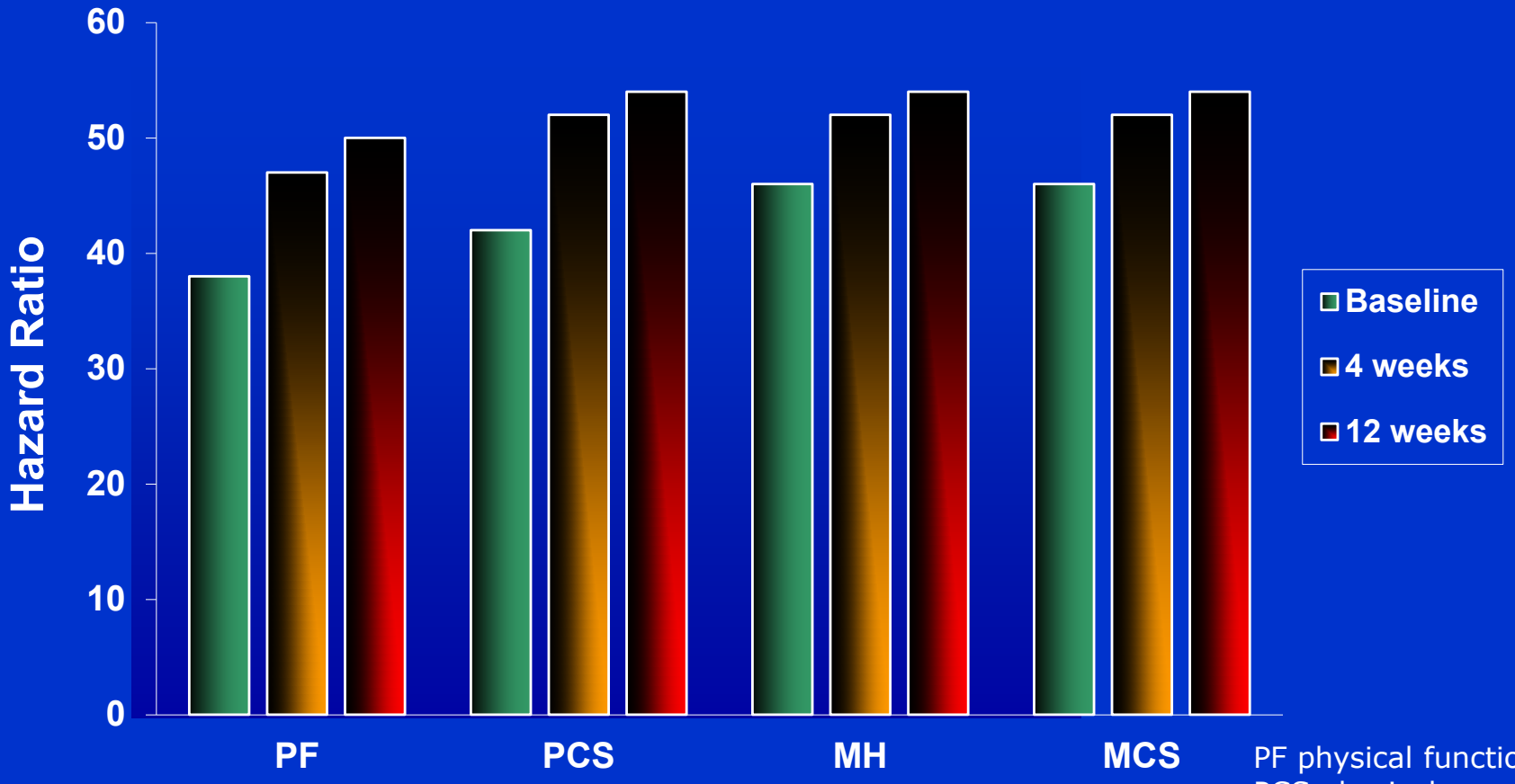
Parretti et al. Obesity Reviews (2016) doi: 10.1111/obr.12366

A qualitative study exploring patient and dietitian experiences with, and perceptions of, a multi-component dietary weight loss program for knee osteoarthritis

- N=24 patients and 5 dietitians
- Ease and convenience (not feeling hungry)
- Social and professional support crucial for success
- Program was engaging and motivating (rapid weight loss)
- Educational resources
- Rewarding experience (less knee pain)

Lawford et al. Osteoarthritis and Cartilage 29 (2021) 507-17

The Effect of Multidisciplinary Supervised Weight Loss on Quality of Life



PF physical function
PCS physical composite
MH mental health
MCS mental composite

Case CC, Endocrine Practice 2004

Association Between Ketosis and Changes in Appetite Markers with Weight Loss Following a Very Low-Energy Diet

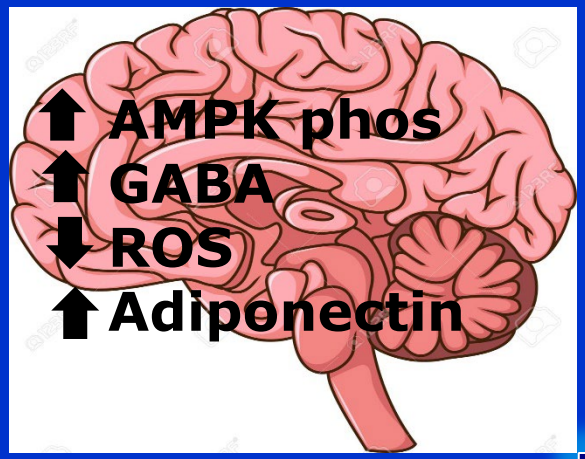
- N=87, BMI 36.5
- VLCD 8 weeks mean weight loss 17.7 kg
- Beta-hydroxybutyrate concentration was negatively associated with ghrelin and positively associated with satiety hormones GLP-1 and CCK.

Martins et al. Obesity (2020) 28, 2331-2338

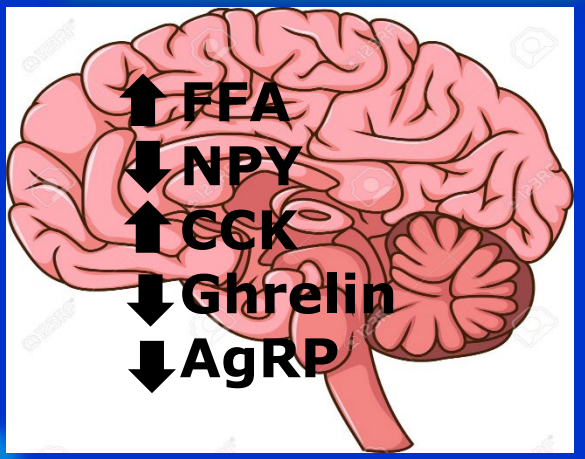
Ketogenic diets/fasting

Increase Blood BHB

Orexigenic



Anorexigenic



Ketones Ester

Increase Blood BHB

Orexigenic

GLP-1
PYY

Anorexigenic

Ghrelin

VLCD and MR

- Weight loss
- Safety
- Structure
- Foundation for weight loss maintenance

Bariatric Endocrinology and Very-Low-Calorie Meal Plans

- 2013 AACE guidelines phase out "diet"
- Very Low Calorie Meal Plans (VLCMP)
- 800 kcal
- Average 12 weeks
- 3-5 lbs/week

Contraindication
MI within 6 months
CVA
Diabetes with DKA
Glucocorticoid use
Active peptic ulcer disease
History of suicide attempt
Active thrombophlebitis
Decreased blood volume
Pregnancy
Occupation requiring alertness
Active Eating disorder
Liver disease
Kidney disease
Hypercoagulable state
Lithium
Age < 13 or > 80
Electrolyte disorders

Gonzalez-Campoy. Endocrine Practice Vol 23 No 6 June 2017

LCD

A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss

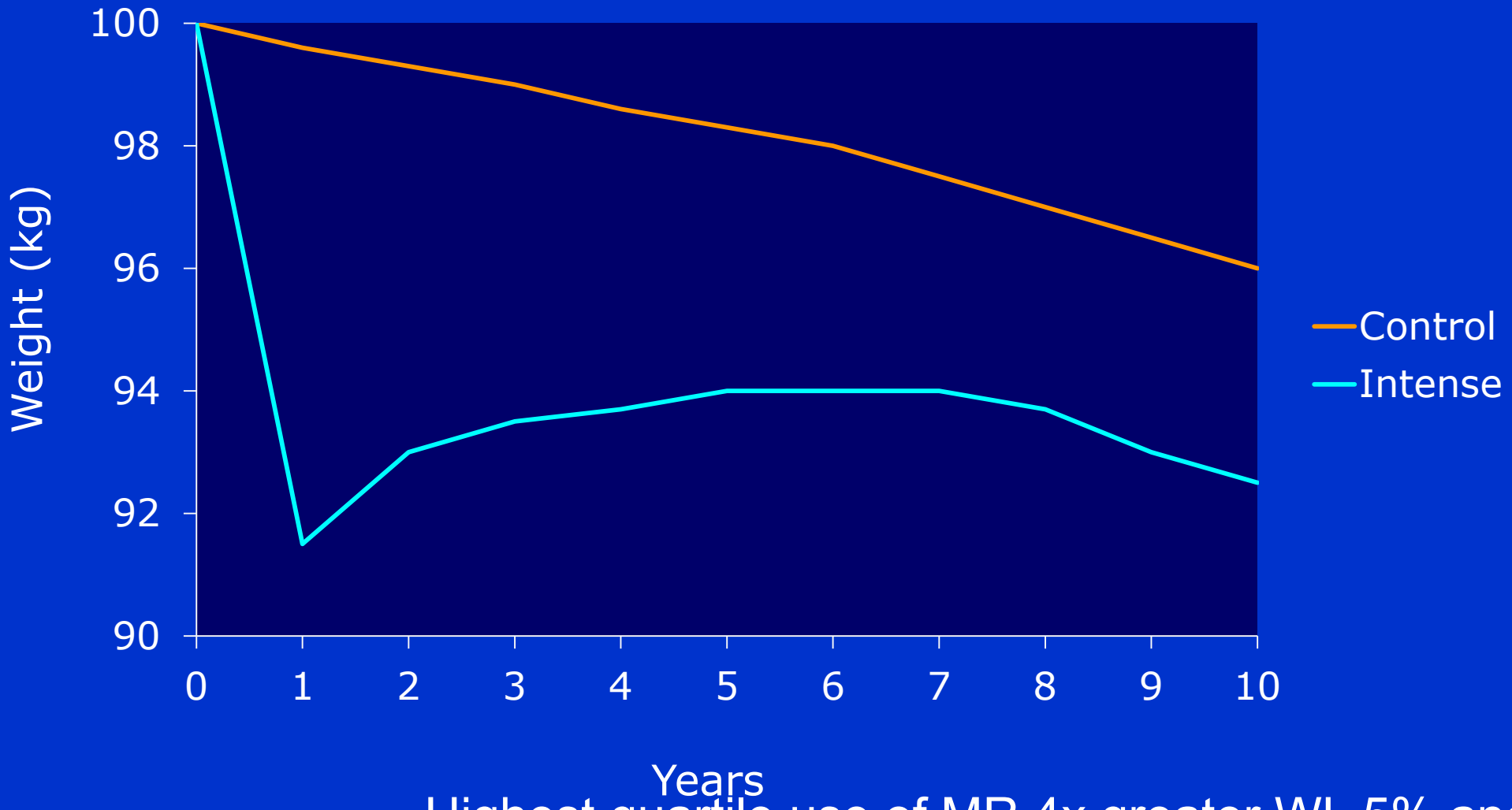
LCD

- Diets incorporating meal replacements with behavior support had 6.3 kg great weight loss compared to regular support without meal replacements at 1 year
- Meal replacement diets 1.44 kg greater weight loss than regular diet
- N=7884, 23 studies

Astbury et al. Obesity Reviews. 2019;20:569-87.

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

The Look AHEAD Study



NEJM 2013;369:145-54

Highest quartile use of MR 4x greater WL 5% and 10%

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

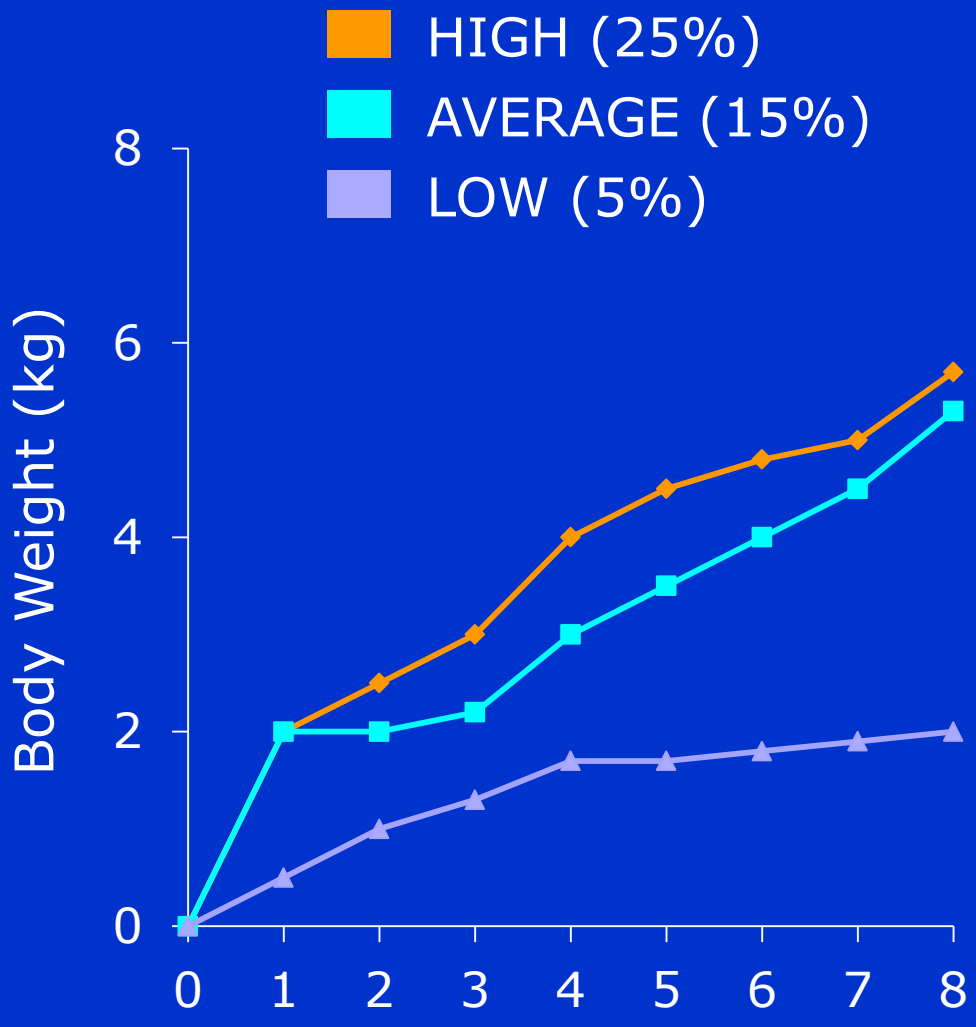
- Greater diabetes remission
- Less kidney disease progression, less retinopathy
- Less depression
- Reduced medications
- Better A1c, weight loss, lipid
- Less sleep apnea
- Lower likelihood to need insulin
- Less urinary incontinence
- Better physical function
- Improvement in QOL

LCD and MR

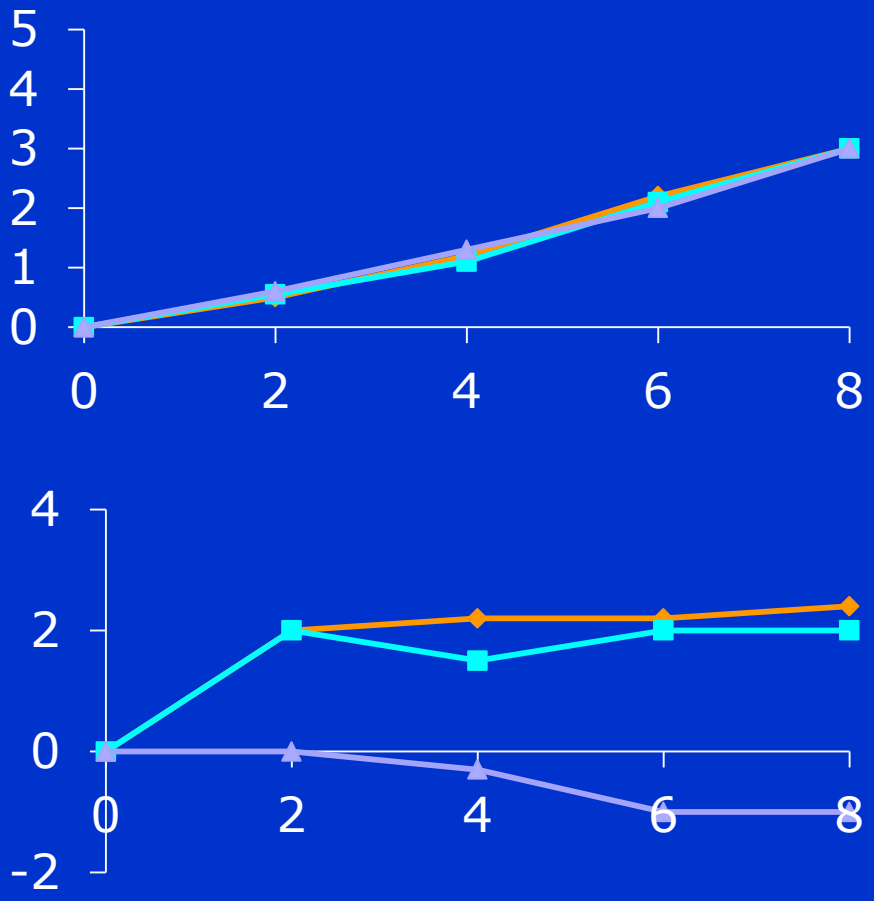
- More effective weight loss
- Structure
- Foundation for weight loss maintenance

Diet

Effect of Dietary Protein Content on Weight Gain, Energy Expenditure, and Body Composition During Overeating



Calories alone contribute to increase in fat, protein contributed to change in energy expenditure and lean body mass but did not increase fat

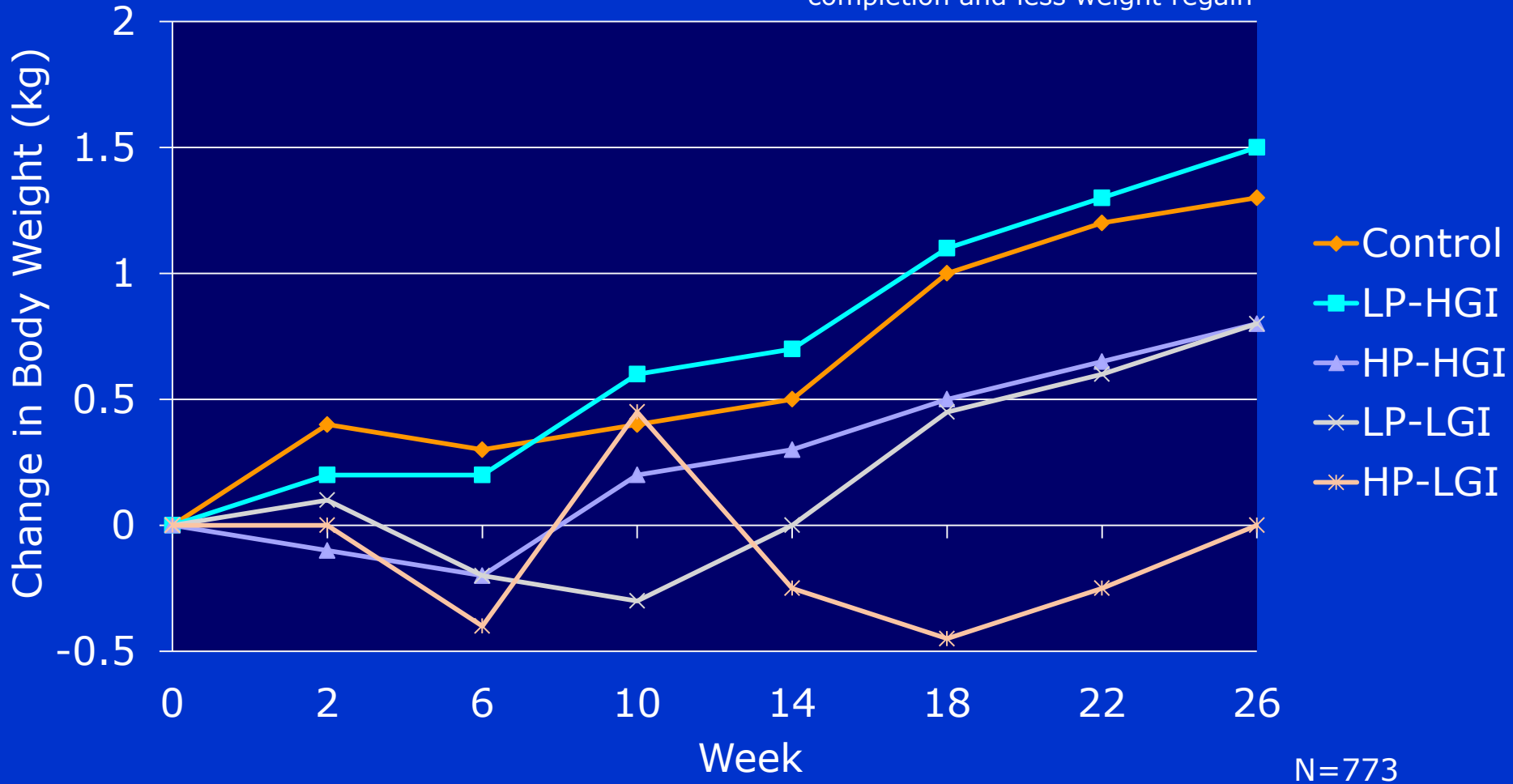


Randomized 5%, 15%, 25% protein
954 kcal overfeeding (140 g/d)
90% low protein stored weight as fat
REE increased in NP and HP

JAMA. 2012;307(1):47-55. doi:10.1001/jama.2011.1918

Diets with High or Low Protein Content and Glycemic Index for Weight-Loss Maintenance

- >8% weight loss with 800 kcal diet
- More protein and reduced glycemic index improved study completion and less weight regain

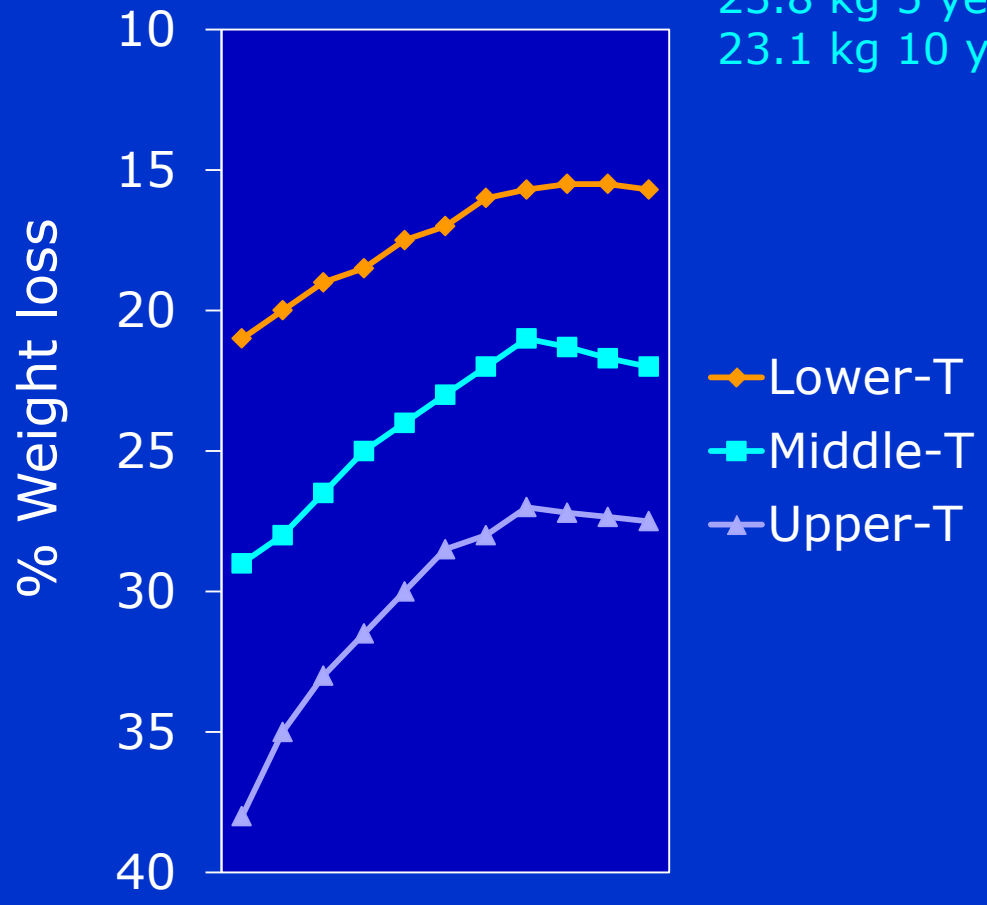


N=773
13% vs 25% protein
-15 Glycemic units

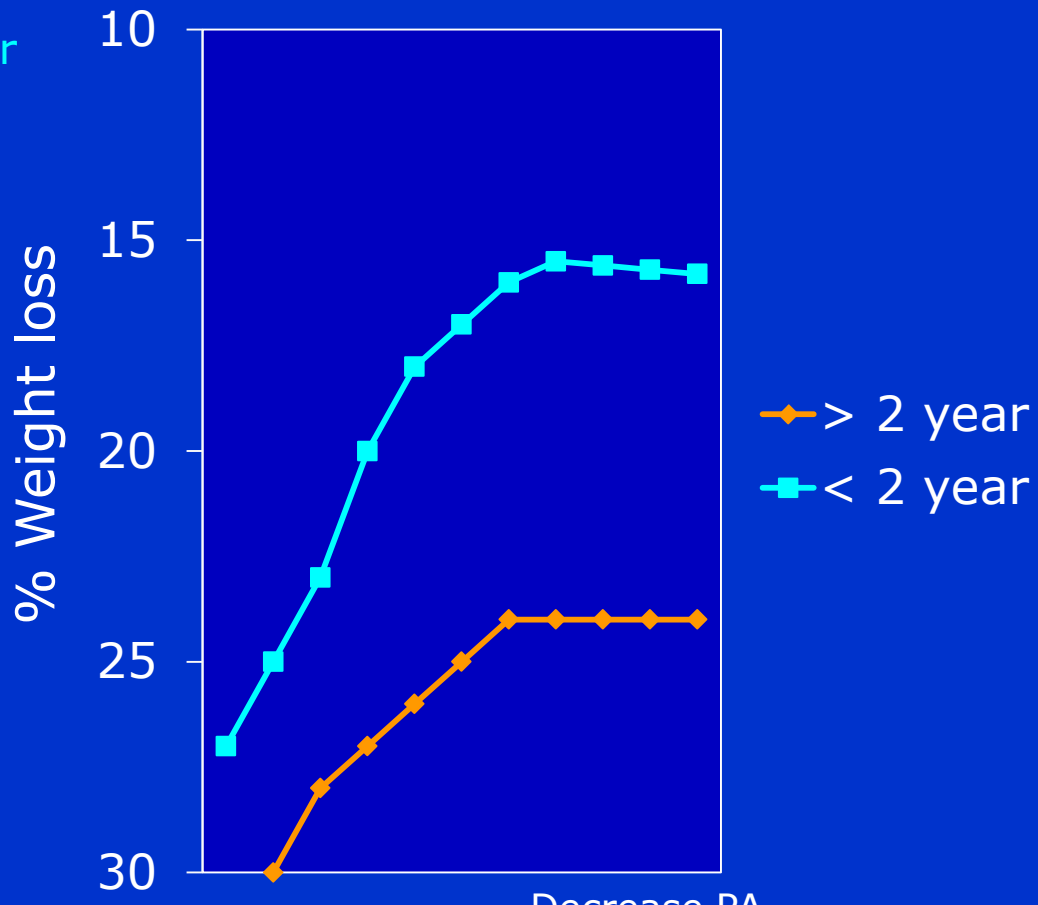
Larsen et al. N Engl J Med 2010;363:2102-13.

Weight-Loss Maintenance for 10 years in the National Weight Control Registry

Mean weight loss
31.3 kg
23.8 kg 5 year
23.1 kg 10 year



Weight loss maintenance becomes less effortful overtime



Decrease PA
Dietary restraint /disinhibition
Frequency of self weighing
Increase in fat intake

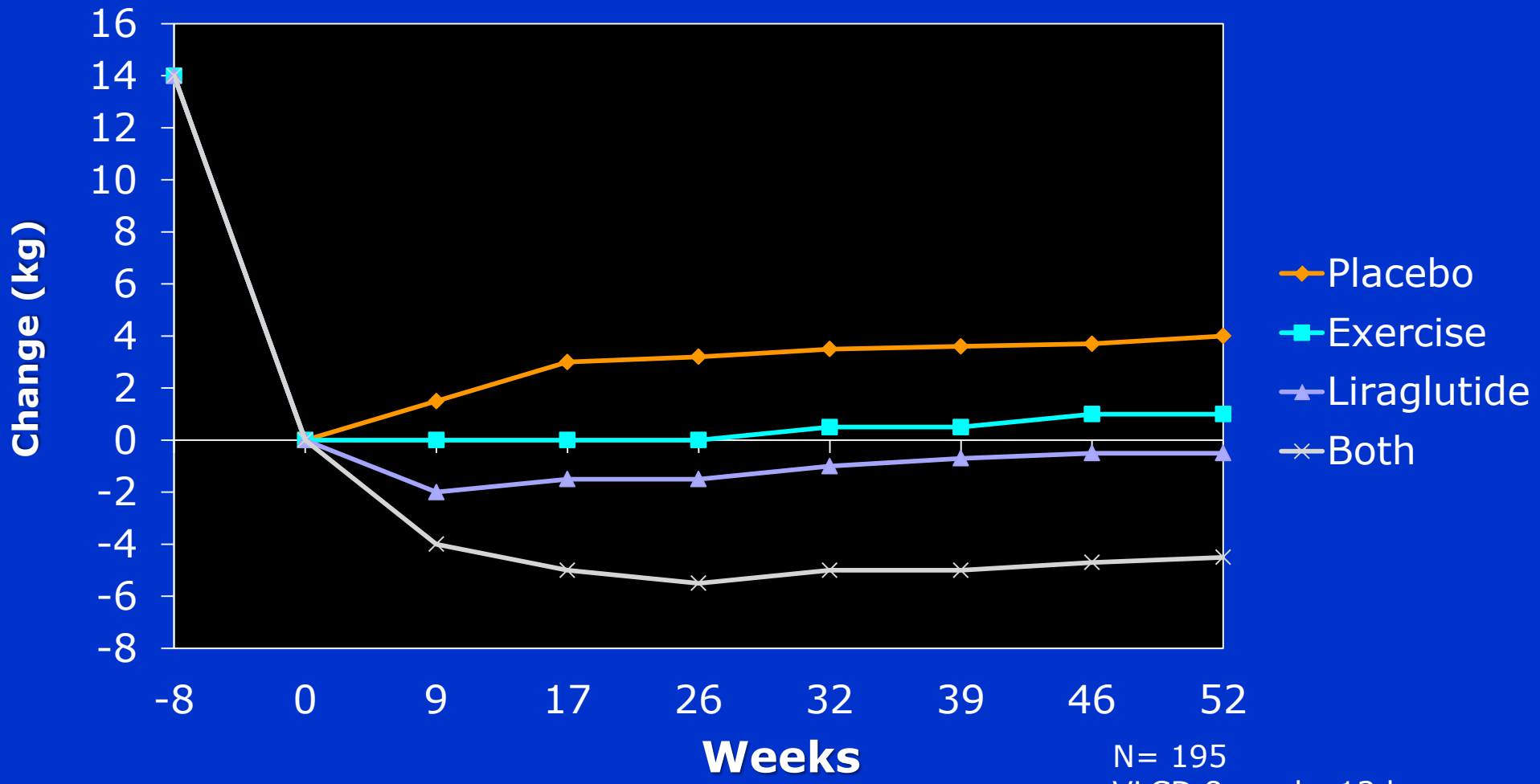
Thomas et al. Am J Prev Med 2014;46(1) 17-23

Diet and MR

- Portion control
- Quality protein
- Structure
- Reduction in food choices

Medications

Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined



N= 195
VLCD 8 weeks 13 kg
BMI 37 age 40

Lundren. NEJM 2021;384:1719-30

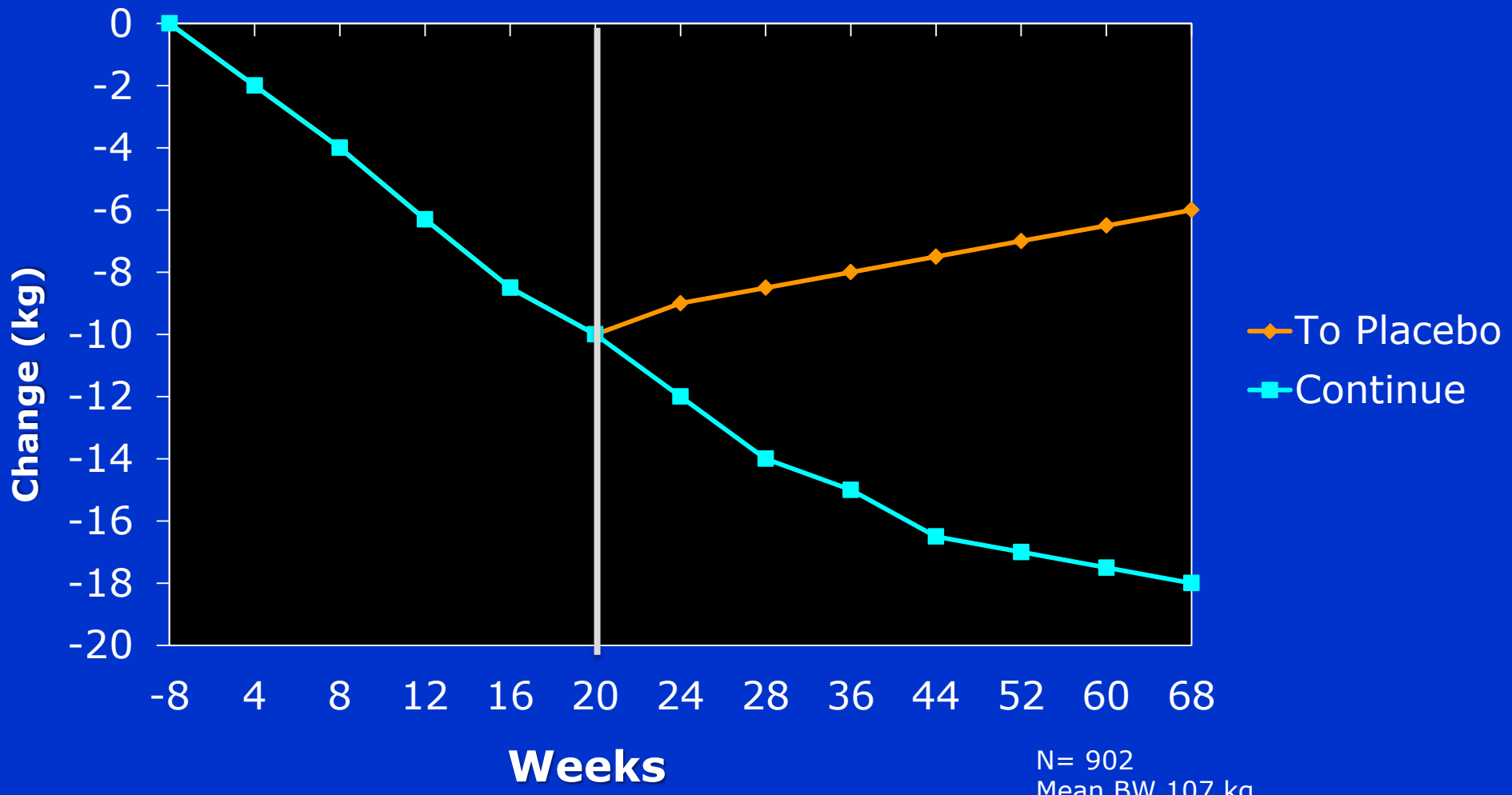
Healthy Weight Loss Maintenance with Exercise, Liraglutide, or Both Combined

	Before	After
Weight (kg)	109.7	96.7
CR fitness (ml/min/kg)	22.9	24.9
Systolic BP (mm/Hg)	132	122
Diastolic BP	86	79
HOMA-IR	3.9	1.7
Cholesterol (mg/dl)	193	158
LDL-C	120	97
Triglycerides	132	97

Improvement in SF-36 physical and emotional well-being

Lundren. NEJM 2021;384:1719-30

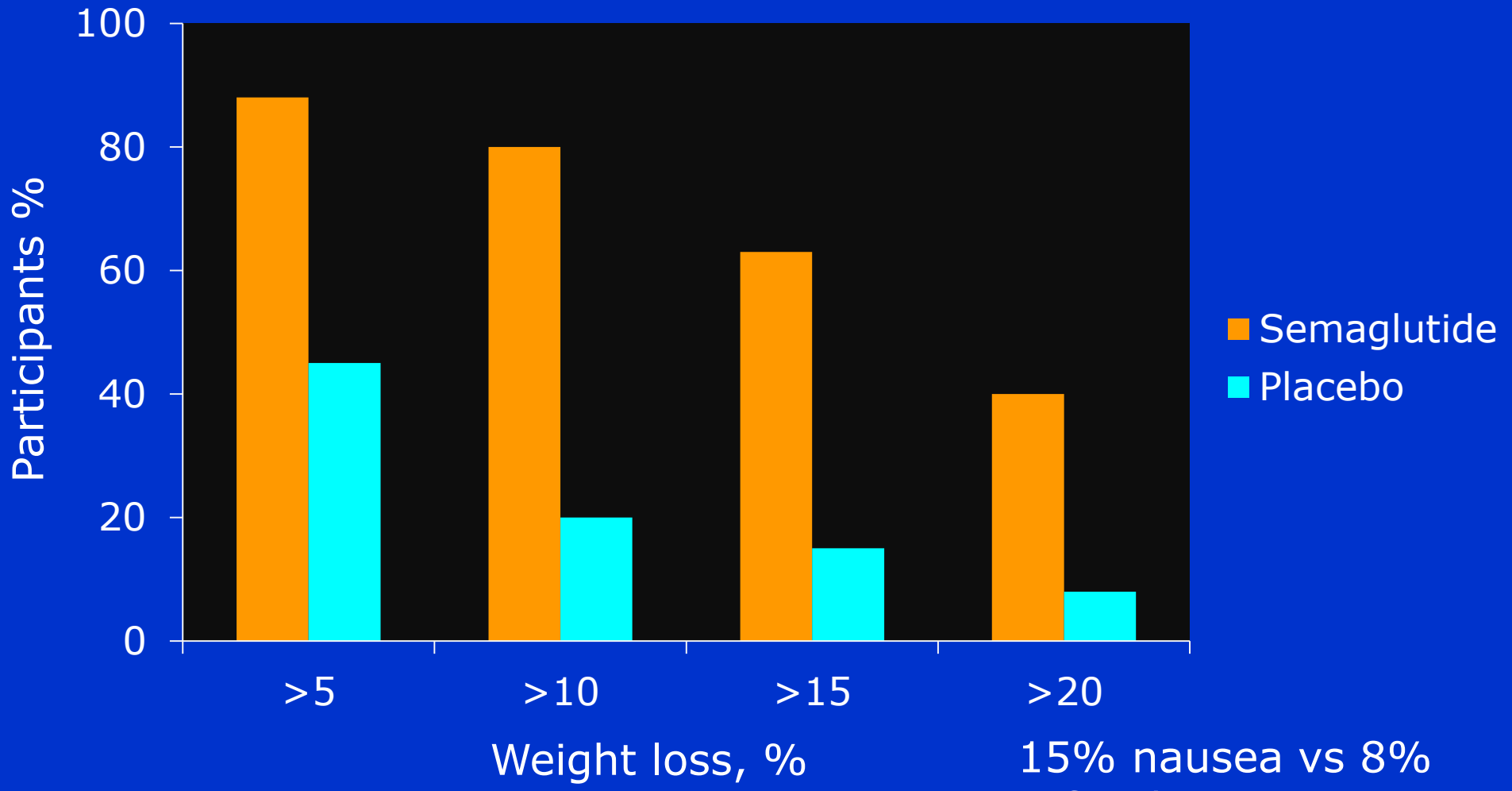
Effect of Continued Weekly Semaglutide vs Placebo on Weight Loss Maintenance in Adults with Overweight or Obesity



N= 902
Mean BW 107 kg
Monthly calls by HCP
Prescribed -500 kcal reduction and 150 min exercise/week

Rubino et al. JAMA 2021 325(14): 1-12

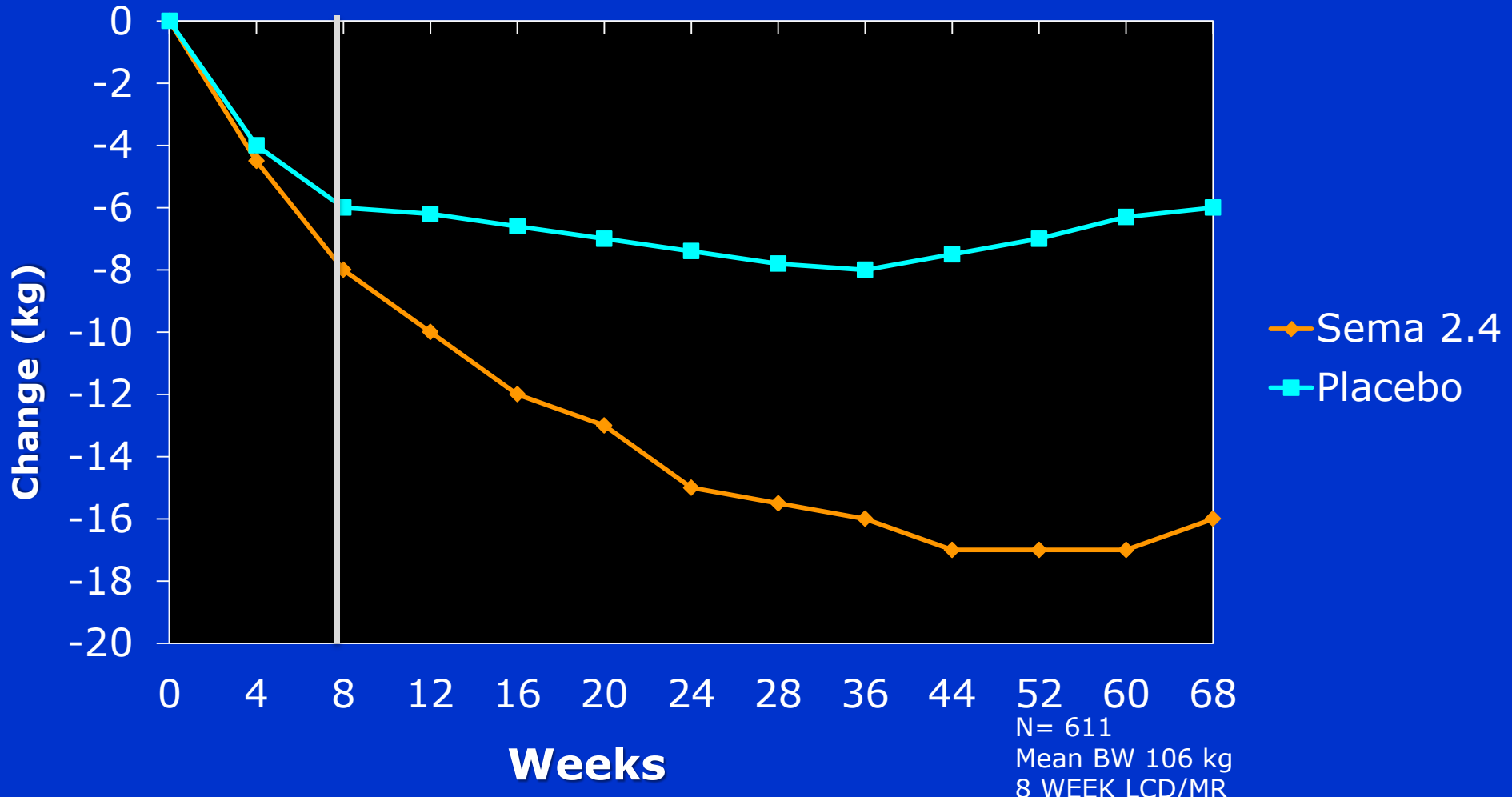
Proportion of participants achieving threshold of weight loss



15% nausea vs 8%
Inflexibility in run in period

Rubino et al. JAMA 2021 325(14): 1-12

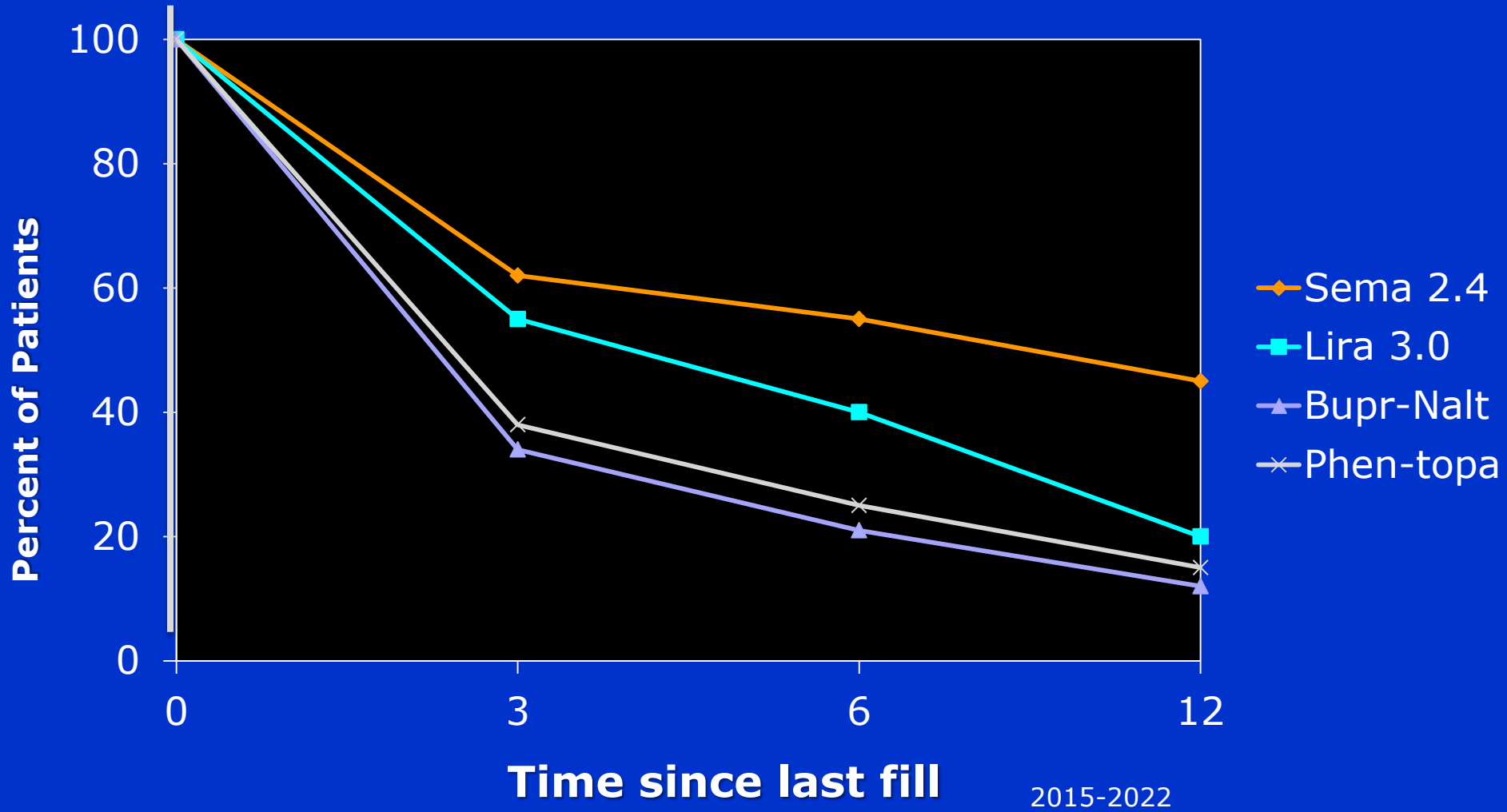
Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity



N= 611
Mean BW 106 kg
8 WEEK LCD/MR
Placebo 47% > 5% weight loss
200 minutes/week
30 RD appt

Rubino et al. JAMA 2021 325(14): 1-12

Early- and later stage persistence with antiobesity medications: A retrospective cohort study

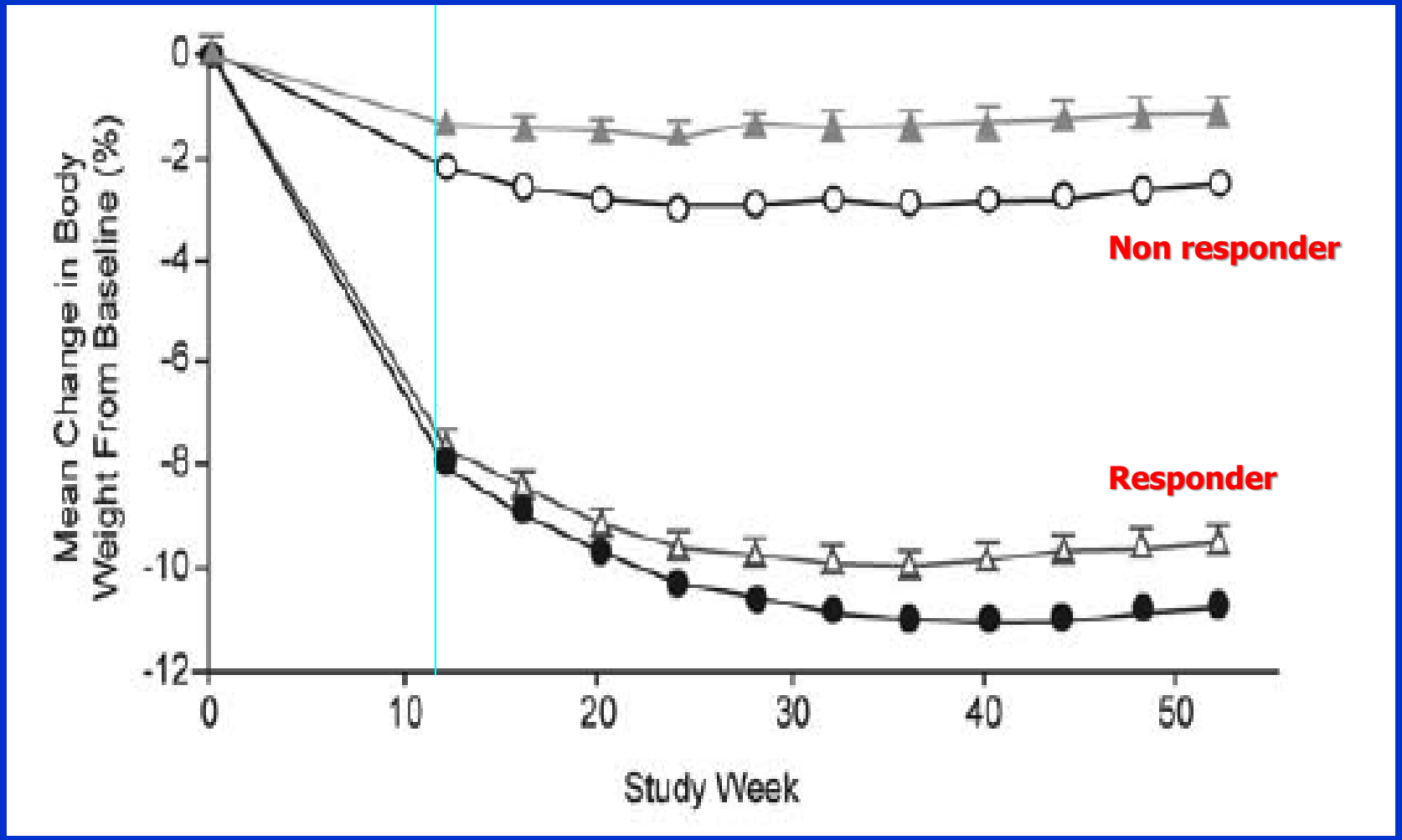


2015-2022
Medical records
1911

Gasoyan et al. Obesity 2023: 1-8

Early weight loss while on locaserin, diet and exercise as a predictor of week 52 weight –loss outcomes

Outcomes by Responder Status



Smith SR, et al. Obesity. 2014;22(10):2137-2146.

Real-world use of once weekly semaglutide in patients with type 2 diabetes

Package insert -3.5kg

Age 60
n-= 1212
Weight 101 kg

BMJ Open Diab Res Care 2022;10

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake

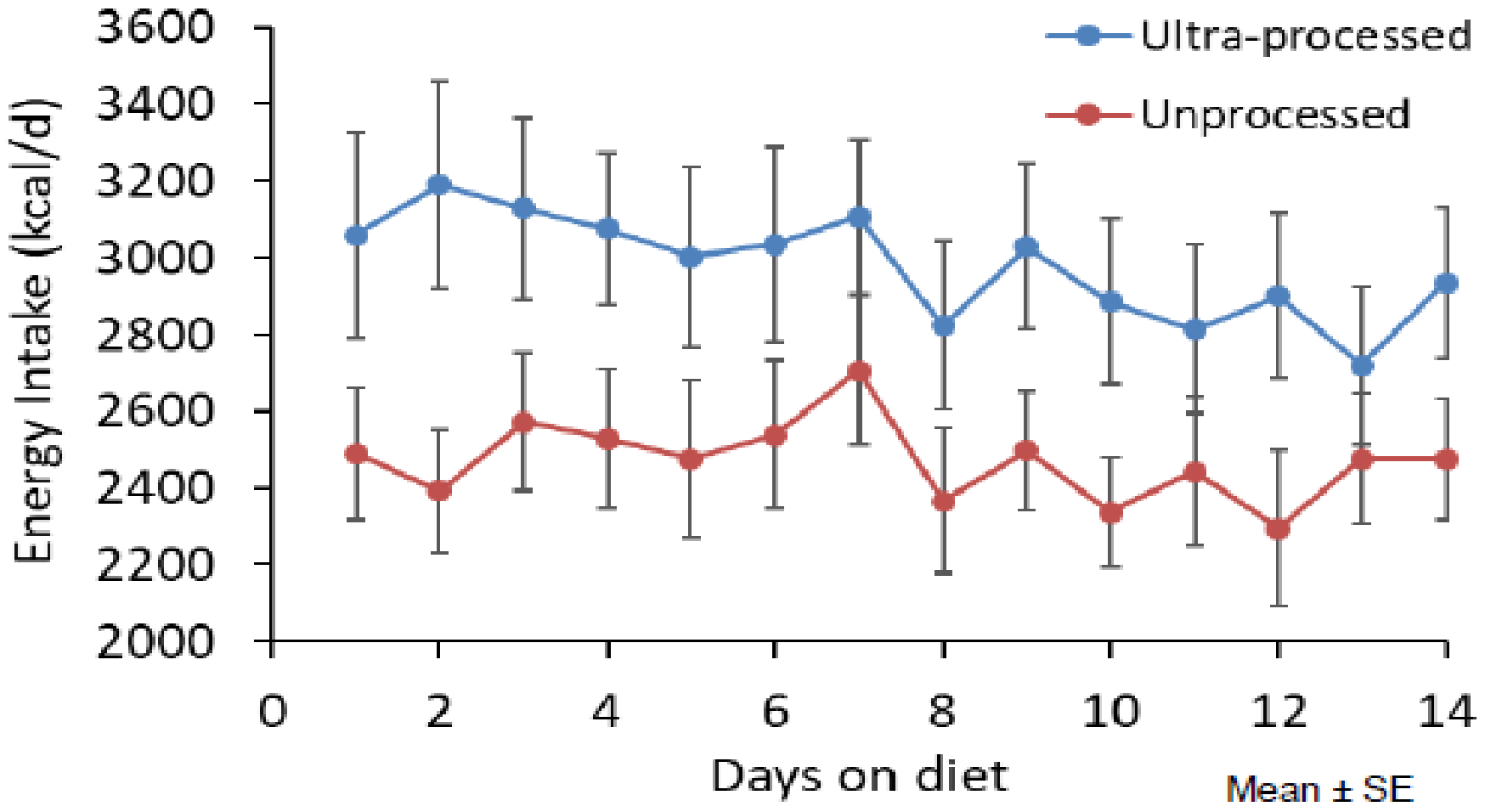
- Eat as much of little as desired
- 7 days of menus
- Diets matched for calories, sugar, fat,fiber, macronutrients
- Primary Outcome: Energy Intake

- MATCHED FOR:
  - Salt
  - Sugar
  - Fat

	Ultra-Processed	Unprocessed
Energy (kcal)	3,905	3,871
Carb (%)	49.2	46.3
Fat (%)	34.7	35.0
Protein(%)	16.1	18.7
Fiber (g/1000 kcal)	21.3	20.7
Energy ultra-processed	83.5	0

Hall et al. Cell Metabolism 30:1-11 (2019)

Ultra-processed Diets Cause Increased Intake



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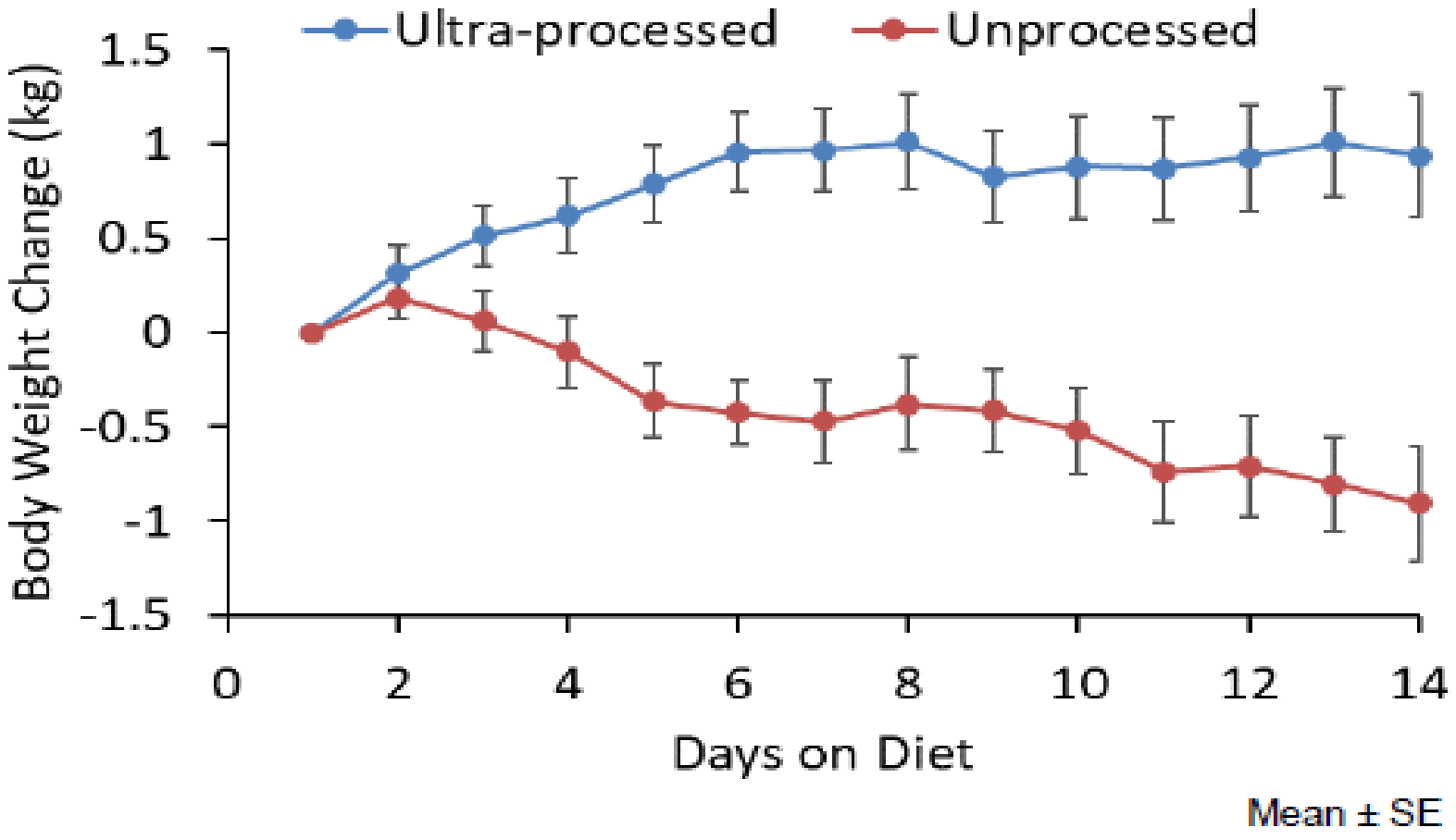
KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Ultra-processed Diets Cause Weight Gain



KD Hall et al. *Cell Metabolism* 30:1-11 (2019).

Meds and MR

- Up to 2x greater weight loss with combination
- Medications alone do address foundation
- Most patients do not achieve desirable weight loss
- Clinical trials have exclusion criteria, motivated patients, aggressive lifestyle beyond clinical practice
- Many patients are non responders
- Medications are lifelong treatments

Wadden TA, et al. Obesity (Silver Spring). 2019;27(1):75-86

Surgery

Patient Behaviors and Characteristics Related to Weight Regain after Roux-en-Y Gastric Bypass

	% of mean weight regain
Eat fast food per meal/week	0.5
Eating when feeling full	2.9
Eating continuously	1.9
Binge eating	8.0
Loss-of-control eating	1.6
Sedentary	2.9
Weighting less than 1 per week	4.2

Mean weight regain 23% at 6.6 years

N=1,278

King WC et al. Ann Surg 2019 DOI: 10.1097/SLA

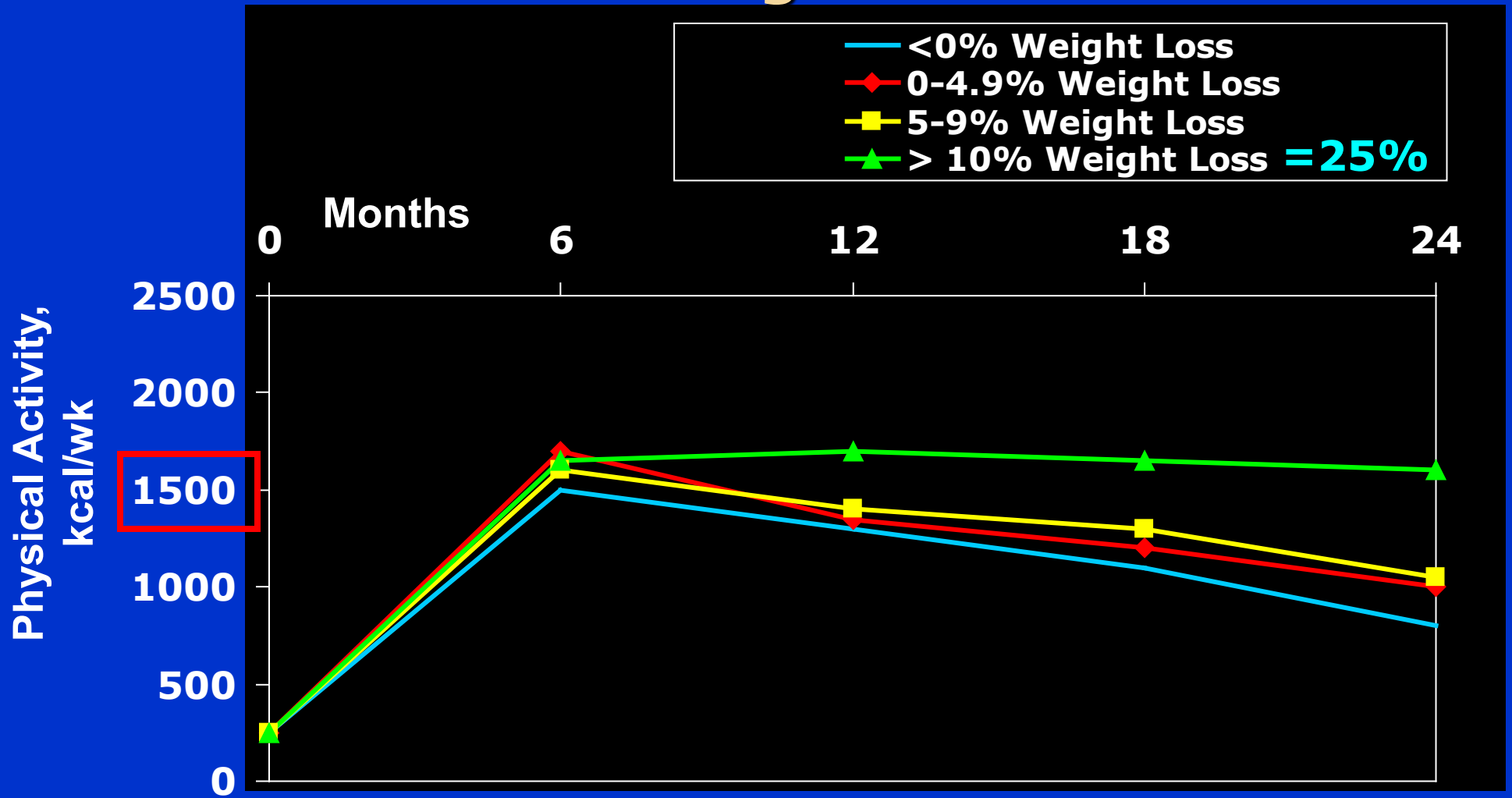
Surgery and MR

- Challenging
- 56% patients regain weight within 10 years of surgery and 25% fail to achieved expected weight loss
- 7% weight regain per year
- Preoperative weight loss
- Postoperative nutrition/protein

Kaouk et al. F1OOOresearch 2020

Exercise

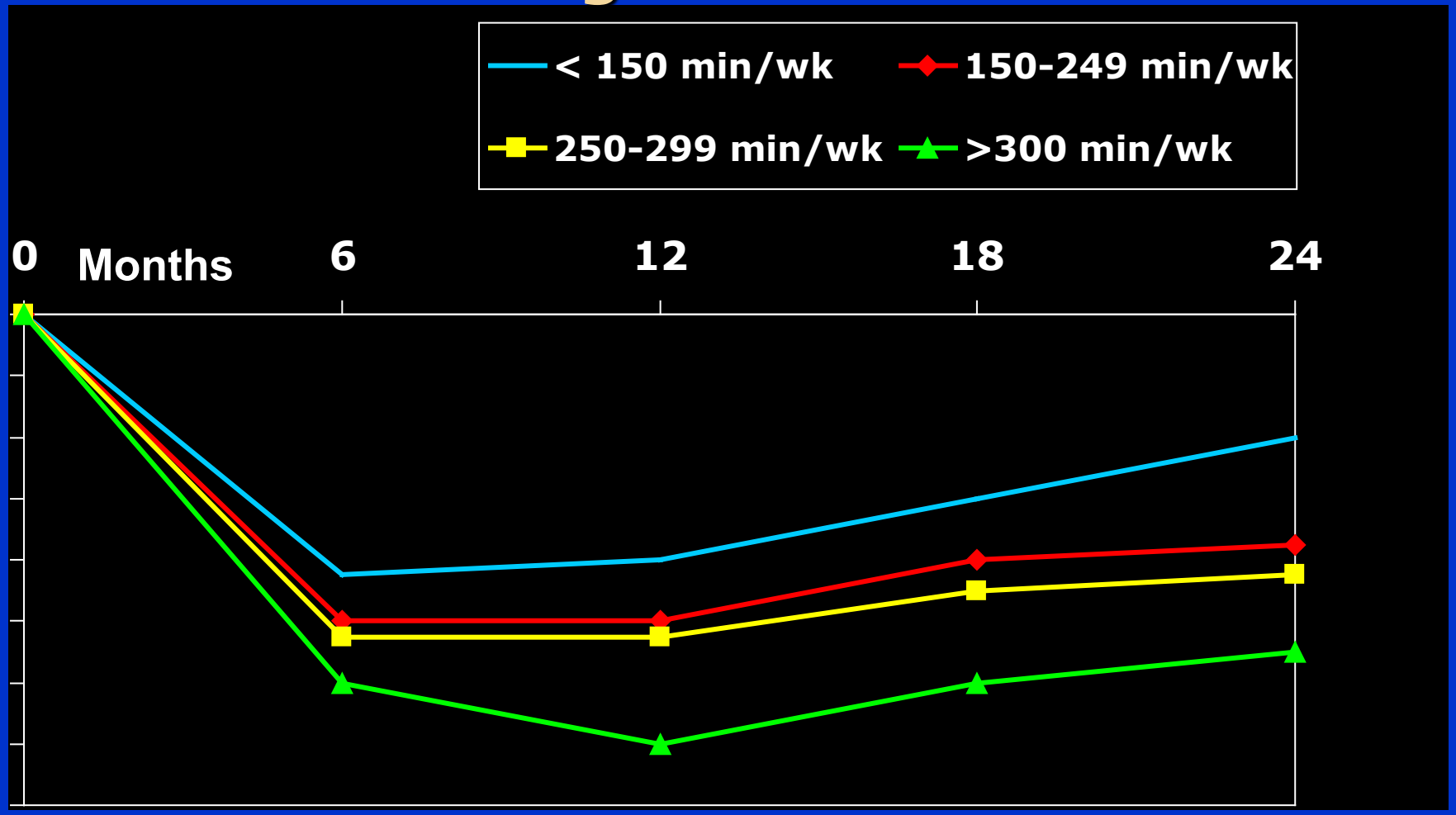
Effect of Exercise on 24-Month Weight Loss Maintenance in Overweight Women



CURRENT +1500 kcal = 275 min/wk

Jakicic et al. Arch Intern Med. 2008;168(14):1550-1559

Effect of Exercise on 24-Month Weight Loss Maintenance in Overweight Women



Jakicic et al. Arch Intern Med. 2008;168(14):1550-1559

Effect of different doses of supervised exercise on food intake, metabolism, and non-exercise physical activity: The E-MECHANIC randomized controlled trial

- Exercise produces less weight loss than expected
- N =198 24 week supervised exercised vs none
- Intake increased 100-125 kcal/d
- -0.4 kg weight loss (700 kcal/week)
- -1.2 kg weight loss (1760kcal/week)

- Increases in intake and appetite

Martin et al. Am J Clin Nutr 2019 (110) 583-592.

Aerobic Physical Activity and Expected Weight Loss

Exercise type	Range of expected Weight loss	Change of clinically significant weight loss
Aerobic only	0-3%	Possible but only high volumes
Resistance only	0-1%	Very unlikely
Both	0-3%	Possible with high aerobic volumes
CR with both	5-15%	Possible

Aerobic PA amount	Weight loss amount
< 150 min per week	None to minimal
150-225 min per week	2-3kg
225-420 min per week	5-7.5 kg
200-300 min per week	WLM after loss

Swift DL et al. Prog Cardio Dis 2018;61(2)206-13
Donnnelly JE et al. Med Sci Sports Exer. 2009;41(2):459-71

Exercise and MR

- Exercise alone typically does not enable weight loss
- Considerable amount/time of exercise to maintain weight

Meal Replacements

- Provide structure improving adherence
- Reduces food choices/decisions
- Portion control
- Greater weight loss and less drop outs with meal replacements compared to conventional diets

Journal of American Dietetic Association. 2009, 330-46.

MR-based LCD greater weight loss than food-based, favoring > 60% of total daily energy intake

Min et al Journal of American Dietitiec Association. 2021 (121) 1551-64.

Meal Replacements

- Part of effective foundation of obesity management
- Quality protein
- Greater weight loss