Obesity and Liraglutide 3.0mg in weight management

Definition and classification of obesity

- Obesity is defined as abnormal or excessive fat accumulation that may impair health
- Body mass index (BMI) provides the most convenient population-level measure of overweight and obesity currently available

$$BMI = \frac{weight\ (kg)}{height\ (m^2)}$$

Classification	BMI (kg/m²)	
	International[1]	Asian population[2,3,4]
Underweight	<18.5	
Normal range	≥18.5 and <25	≥18 and <23
Pre-obesity*	≥25 and <30	≥23 and <25
Obesity	≥30	>25
Obesity class I	≥30 and <35	
Obesity class II	≥35 and <40	
Obesity class III	≥40	

*previously described as overweight
BMI, body mass index

1. WHO. Factsheet . Accessed on June 2019; 2. Misra, A., et al. *J Assoc Physicians India* 2009; 57:163–70; 3. Kubota, Y., et al., *J Epidemiol,* 2015. 25(8): 553-8; 4. Ota, T., et al., *Diabetes Care,* 2002. 25(7): 1252-3.

Waist circumference as a measure of obesity

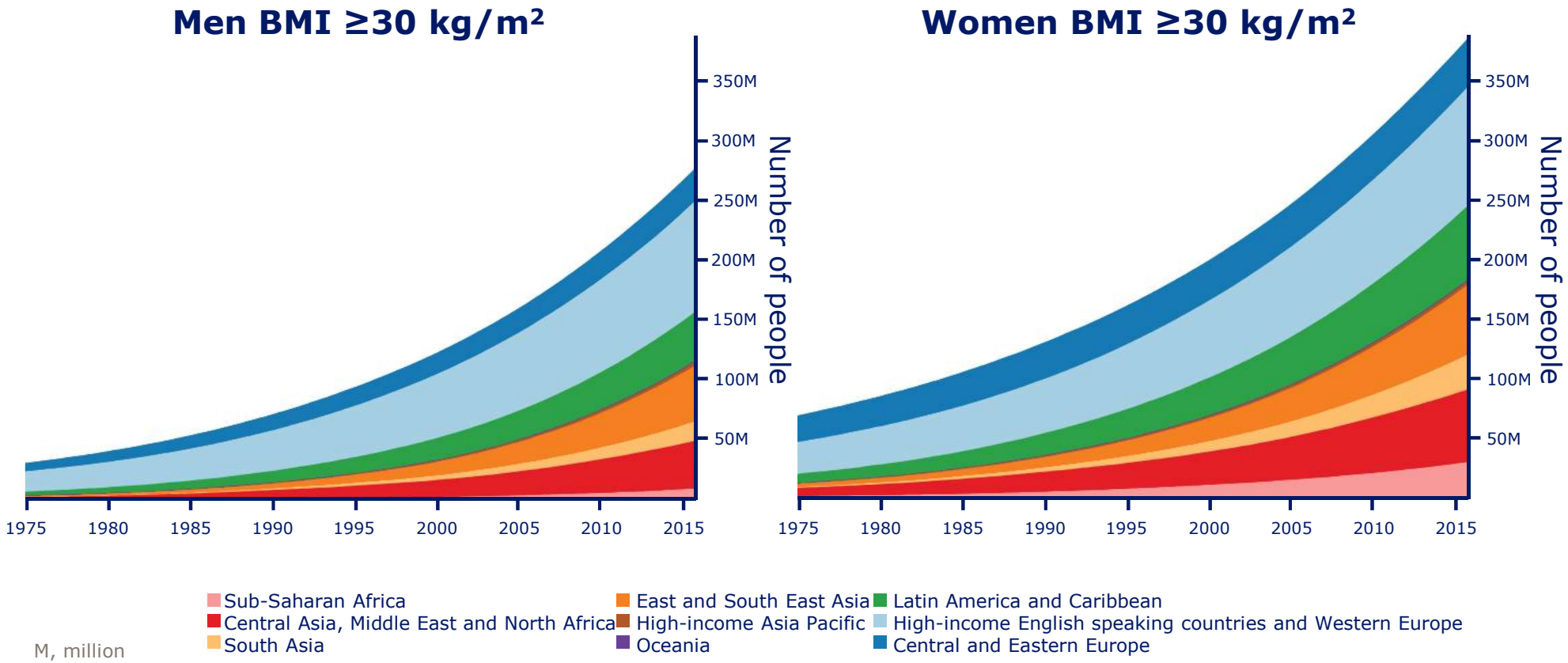
- Waist circumference helps to screen health risks of obesity and overweight
- This risk goes up with a waist size that is greater than 35 inches for women or greater than 40 inches for men

Classification	BMI (kg/m²)	Disease risk relative to normal weight	
		Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >5 in (88 cm)
Pre-obesity*	≥25 and <30	Increased	High
Obesity			
Obesity class I	≥30 and <35	High	Very high
Obesity class II	≥35 and <40	Very high	Very high
Obesity class III	≥40	Extremely high	Extremely high

* previously described as overweight according to WHO nomenclature
BMI, body mass index

NIH, National Heart, Lung and Blood Institute. https://www.nhlbi.nih.gov/health/educational/lose_wt/risk.htm (accessed on May 2019); WHO. Factsheet . Accessed on June 2019

Obesity rates worldwide are increasing



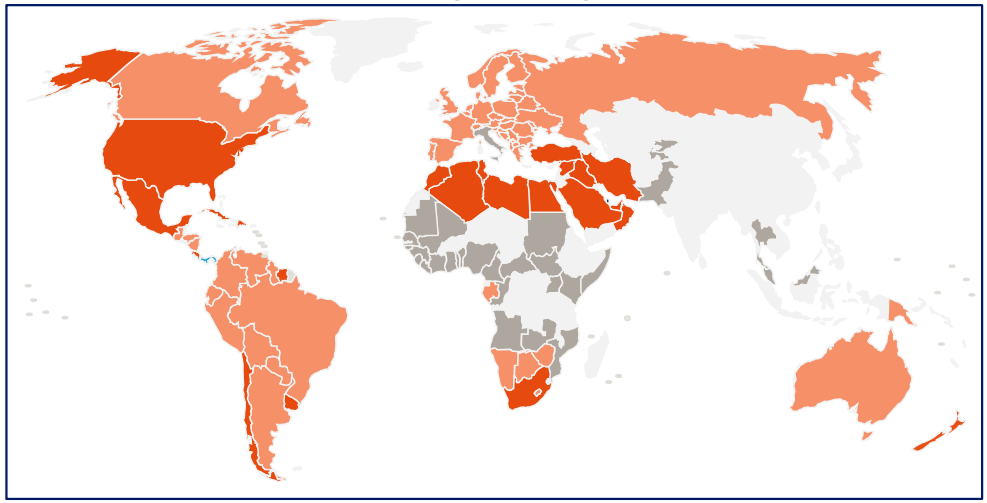
M, million

Adapted from NCD Risk Factor Collaboration (NCD-RisC). *Lancet* 2017:390;2627–42

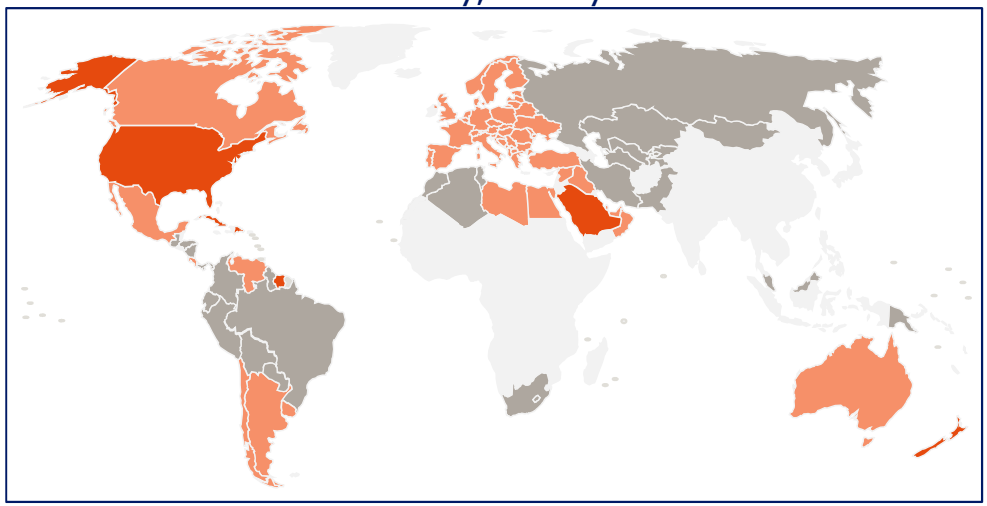
Global prevalence of obesity: 2016

Age-standardised adjusted estimates for adults with BMI ≥30 kg/m^2

Prevalence of obesity, >18 years – Female[1]



Prevalence of obesity, >18 years – Male[2]



Prevalence (%) ≥30 20 – 29.9 10.0 – 19.9 <10.0 or no data available

BMI, body mass index

1. World Health Organisation, Prevalence of obesity in ages 18+ females , 2016. Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_Obesity_2016_Female.png (Last accessed: February 2019); 2.World Health Organisation, Prevalence of obesity in ages 18+ males, 2016. Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_Obesity_2016_Male.png (Last accessed: February 2019).

Obesity is recognised as a disease and health issue

WOF

"WOF takes the position that obesity is a chronic, relapsing, progressive disease process and emphasizes the need for immediate action for prevention and control of this global epidemic"[1]

World Obesity Federation

OC

"Obesity is characterized by excess body fat that can threaten or affect your health. Many organizations including Obesity Canada, now consider obesity to be a chronic disease."[4]

Obesity Canada

AMA

"AMA recognizes obesity and overweight as a chronic medical condition (de facto disease state) and urgent public health problem…and work towards the recognition of obesity intervention as an essential medical service…"[2]

American Medical Association

EASO

"A progressive disease, impacting severely on individuals and society alike, it is widely acknowledged that obesity is the gateway to many other disease areas…"[5]

European Association for the Study of Obesity

RCP UK

"It is important to the health of the nation that we remove the stigma associated with obesity. It is not a lifestyle choice caused by individual greed but a disease caused by health inequalities, genetic influences and social factors.."

Royal College of Physicians UK

1. Bray *et al. Obes Rev* 2017;18:715–23; 2. AMA resolutions. June 2012. Available here; 3. Obesity Canada. Available here; 4. EASO: 2015 Milan Declaration: A Call to Action on Obesity. Available here. Last accessed: June 2019; 5. Royal College of Physicians. Anon. *BMJ* 2019;364:l45; https://www.rcplondon.ac.uk/news/rcp-calls-obesity-be-recognised-disease

Obesity meets common criteria of a disease

AMA	• An impairment of the normal functioning of some aspect of the body • Characteristic signs or symptoms • Harm or morbidity

Obesity

- Appetite dysregulation
- Abnormal energy balance
- Endocrine dysfunction
- Infertility
- NAFLD
- Dyslipidaemia

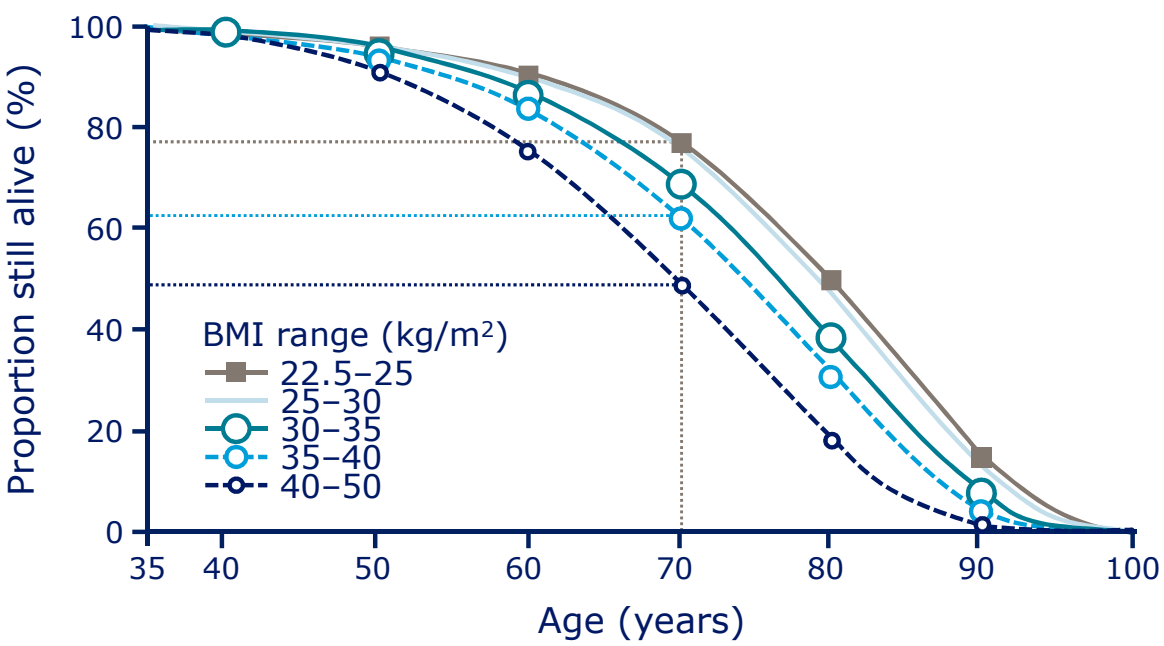
- Increased body fat
- Symptoms associated with increased body fat including:
  - Joint pain
  - Immobility
  - Sleep apnoea

- Type 2 diabetes
- Cardiovascular disease
- Cancer
- Osteoporosis
- Polycystic ovary syndrome

AMA, American Medical Association, NAFLD, non-alcoholic fatty liver disease

American Medical Association Resolution: 420 (A-13). Available at: http://www.npr.org/documents/2013/jun/ama-resolution-obesity.pdf.

Life expectancy decreases as BMI increases



Normal BMI = almost 80% chance of reaching age 70

BMI 35–40 = ~60% chance of reaching age 70

BMI 40–50 = ~50% chance of reaching age 70

Data are based on male subjects; n=541,452

Prospective Studies Collaboration. *Lancet* 2009;373:1083–96

Obesity is associated with multiple comorbidities and complications

Metabolic, mechanical and mental

Metabolic

Mechanical

Mental

Depression

Anxiety

Asthma

NAFLD

Gallstones

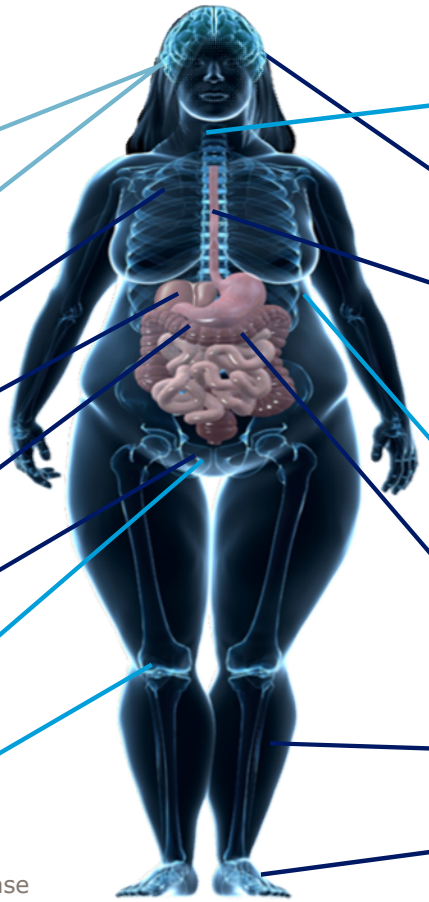
Infertility

Incontinence

Arthrosis

Cancers*

Physical functioning



Sleep apnoea

CVD and risk factors
- Stroke
- Dyslipidaemia
- Hypertension
- Coronary artery disease
- Congestive heart failure
- Pulmonary embolism

Chronic back pain

Type 2 diabetes
Prediabetes

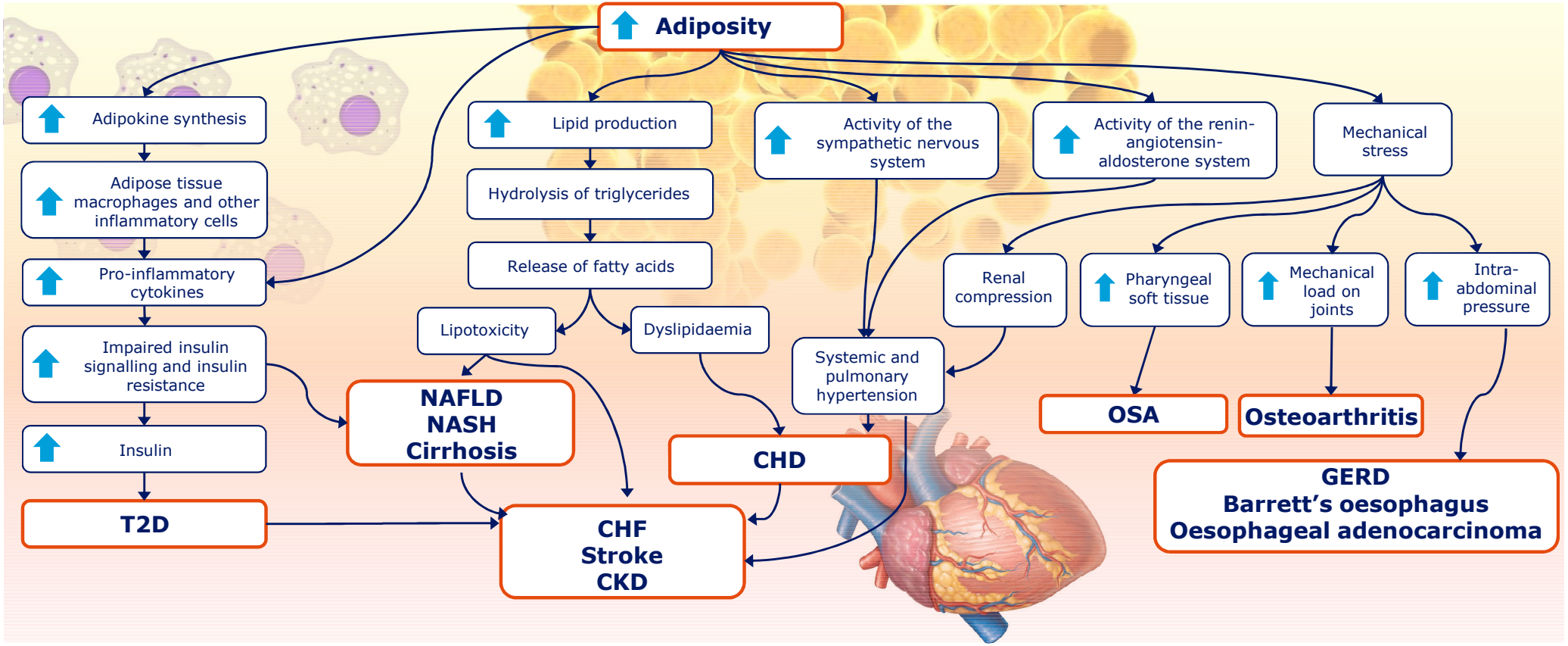
Thrombosis

Gout

CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease
*Including breast, colorectal, endometrial, esophageal, kidney, ovarian, pancreatic and prostate

Adapted from Sharma AM. *Obes Rev*. 2010;11:808-9; Guh *et al. BMC Public Health* 2009;9:88; Luppino *et al. Arch Gen Psychiatry* 2010;67:220–9; Simon *et al. Arch Gen Psychiatry* 2006;63:824–30; Church *et al. Gastroenterology* 2006;130:2023–30; Li *et al. Prev Med* 2010;51:18–23; Hosler. *Prev Chronic Dis* 2009;6:A48

Excess adiposity leads to major risk factors and common chronic diseases



CHD, coronary heart disease; CHF, coronary heart failure; CKD, chronic kidney disease; GERD, gastroesophageal reflux disease; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic stereohepatitis; OSA, obstructive sleep apnea; T2D, type 2 diabetes. Heymsfield SB, Wadden TA. *NEJM* 2017;376:254–66

Greater weight loss further improves obesity-related complications

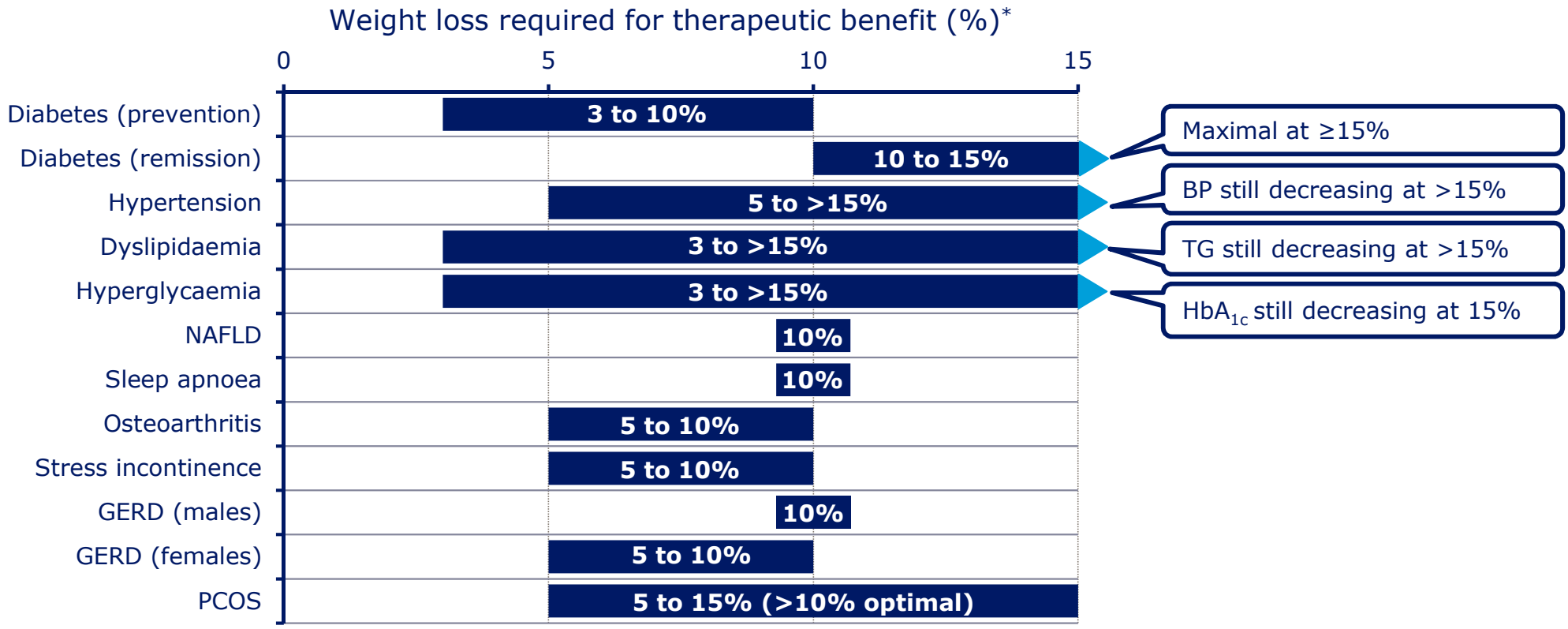
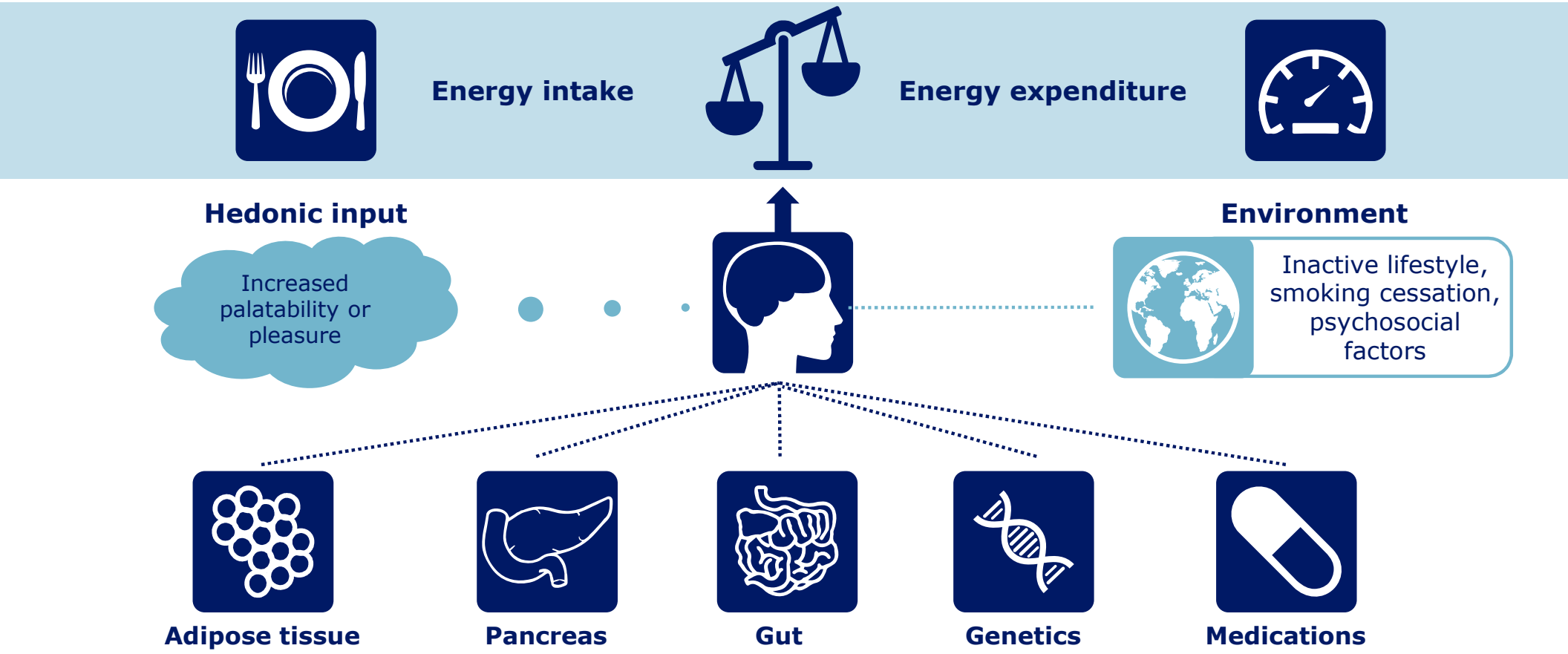


*Figure displays weight loss ranges examined in the studies (impact of >10% weight on NAFLD, and sleep apnoea symptoms was not reported). BP, blood pressure; TG, triglycerides; GERD, gastroesophageal reflux disease; NAFLD, non-alcoholic fatty liver disease; PCOS, polycystic ovary syndrome; TG, triglycerides

Cefalu *et al*. *Diabetes Care* 2015;38:1567–82; Lean *et al. Lancet* 2018;391:541–51

Obesity is a complex and multifactorial disease



1. Badman, Flier. *Science* 2005;307:1909–14; 2. US Department of Health and Human Services, 1998. NIH Publication No. 98-4083

Homeostatic vs. hedonic regulation of appetite

Homeostatic regulation

Biological systems that acts to **maintain** body weight by:

- Regulation via peptide hormones that can induce hunger/satiety
- Changes in energy expenditure

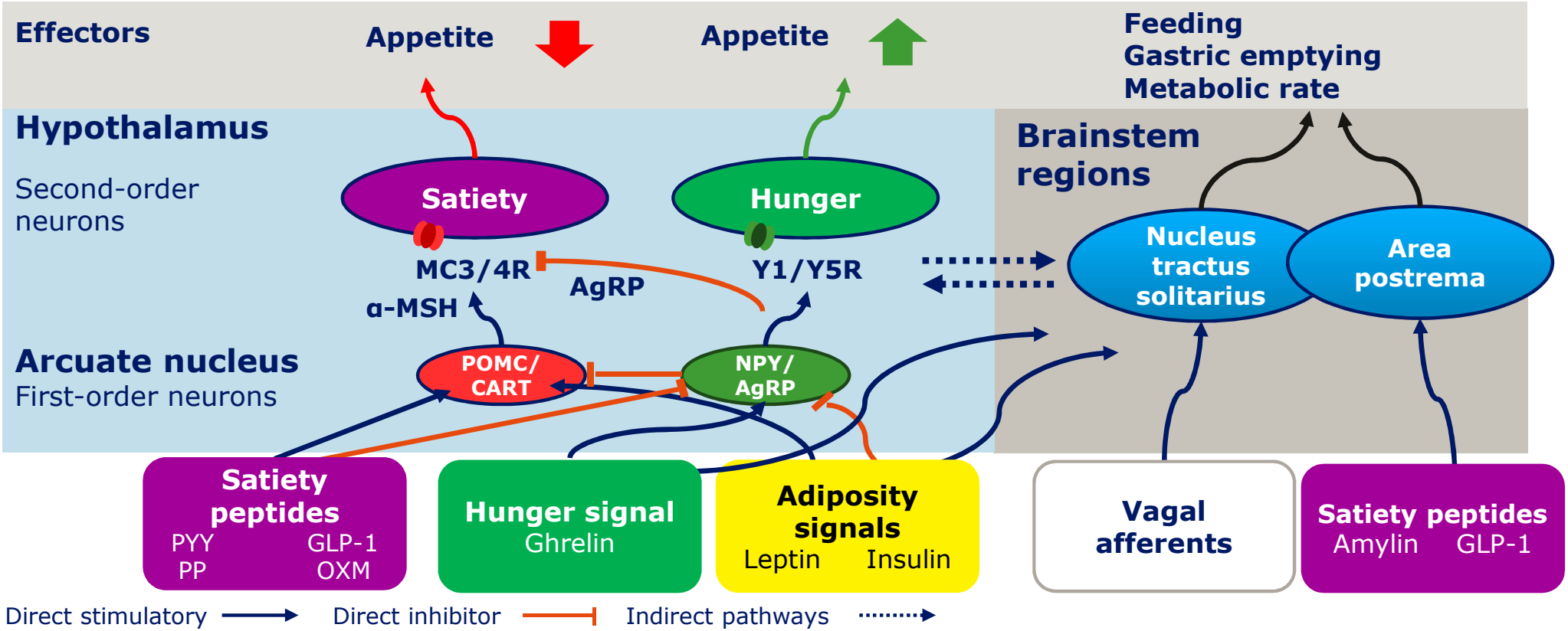
Hedonic regulation

Reward of **survival behaviours** (e.g. sex or eating) through **pleasure**

- Operates even in the presence of satiety signals
- Can lead to food consumption beyond homeostatic need
- Link between hedonic attraction to high calorie foods and obesity

Hall et al. *Am J Public Health* 2014; 104(7): 1169-1175

Homeostatic regulation of appetite



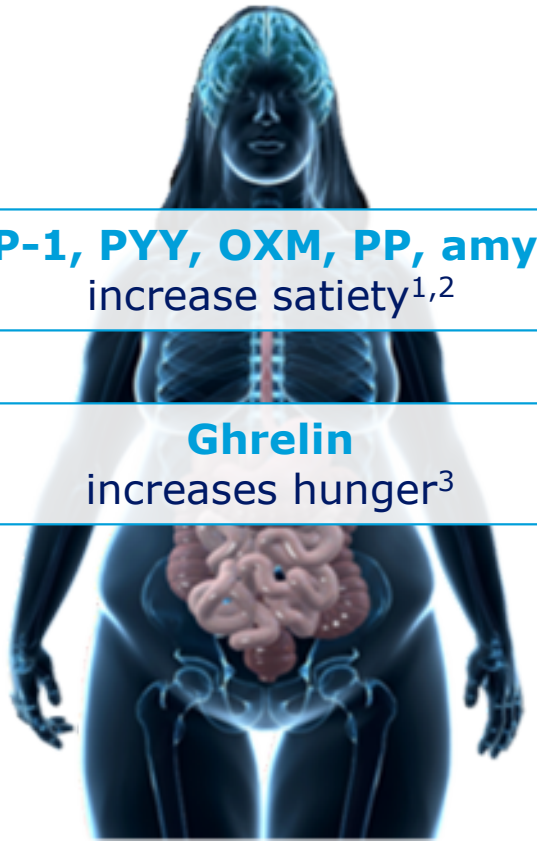
α-MSH, α-melanocyte stimulating hormone; AgRP, Agouti-related peptide; CART, cocaine- and amphetamine-regulated transcript; GLP-1, glucagon-like peptide-1; MC3/4R, melanocortin 3/4 receptor; NPY, neuropeptide Y; OXM, oxyntomodulin; POMC, pro-opiomelanocortin; PP, pancreatic polypeptide; PYY, peptide YY; Y1/Y5R, Y1/Y5 receptor.

Adapted from: Badman et al. *Science* 2005;307:1909–14; Seo et al. *Endocr J* 2008;55:867–74; Secher et al. *J Clin Invest* 2014;124:4473–88.

The role of the brain in controlling eating

Homeostatic eating

'eating for hunger'



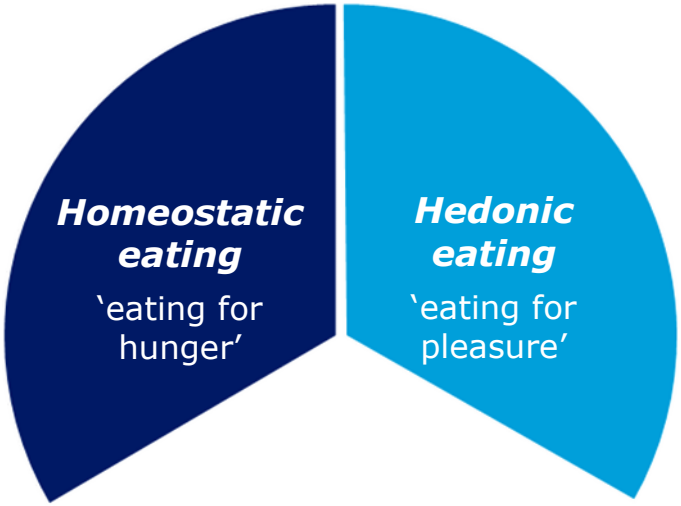
GLP-1, PYY, OXM, PP, amylin
increase satiety[1,2]

Ghrelin
increases hunger[3]

GLP-1, glucagon-like peptide-1; POMC, pro-opiomelanocortin; PP, pancreatic polypeptide; PYY, peptide YY; OXM, oxyntomodulin

1. Badman *et al. Science* 2005;307:1909–1914; 2. van Bloemendaal *et al. Diabetes* 2014;63:4186–4196; 3. Klok *et al. Obes Rev* 2007;8:21–34

The role of the brain in controlling eating

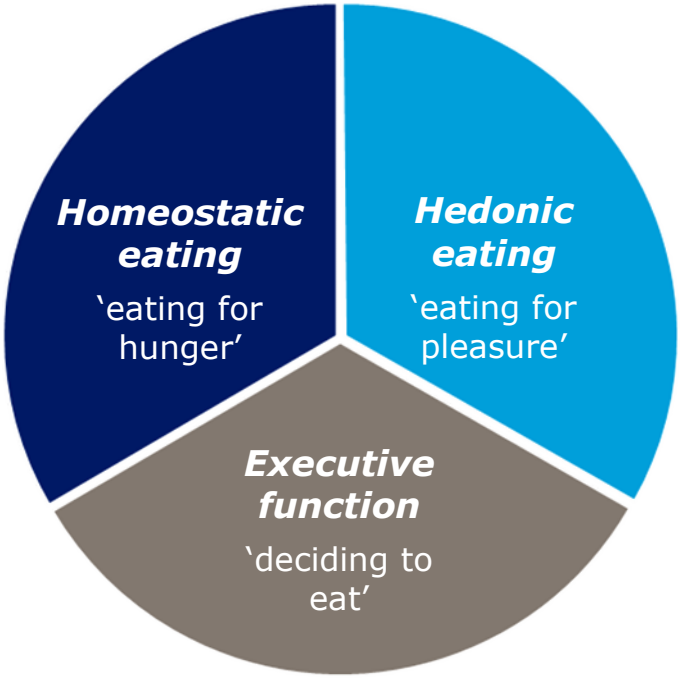


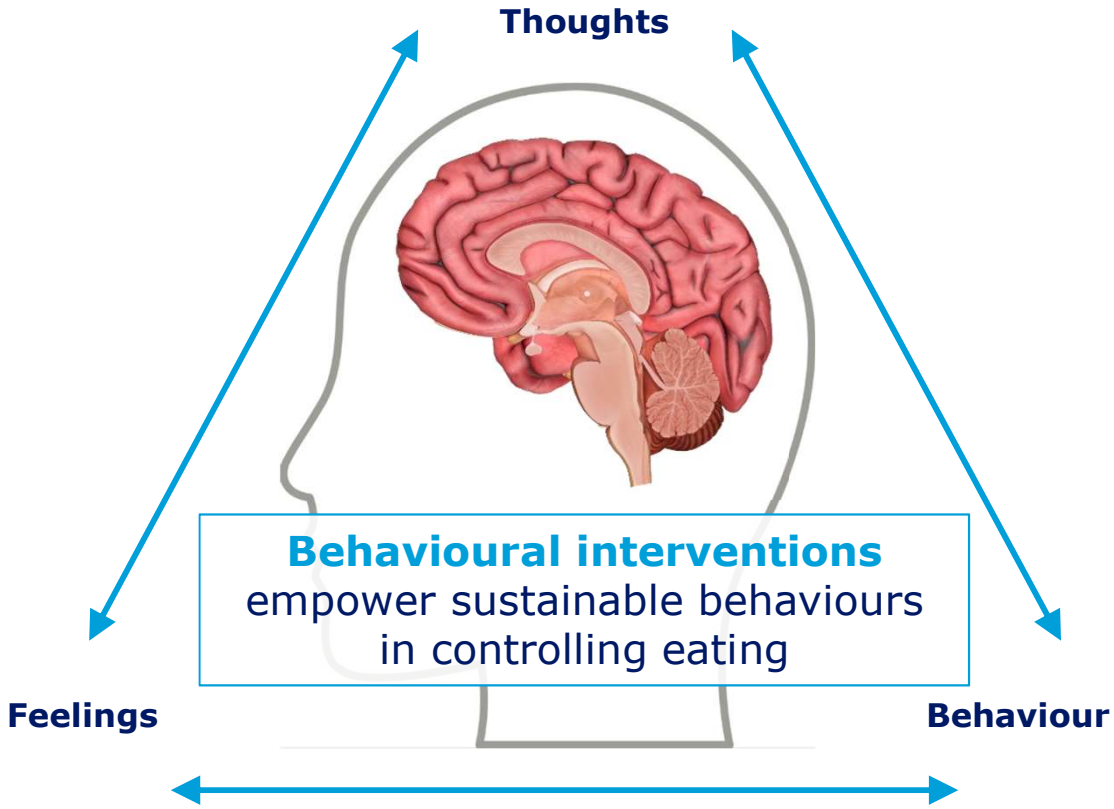
Dopamine controls WANTING, the motivation/drive to eat

Opioid and cannabinoid receptors control LIKING, the pleasure associated with food

Berridge *et al. Brain Res* 2010;1350:43–64

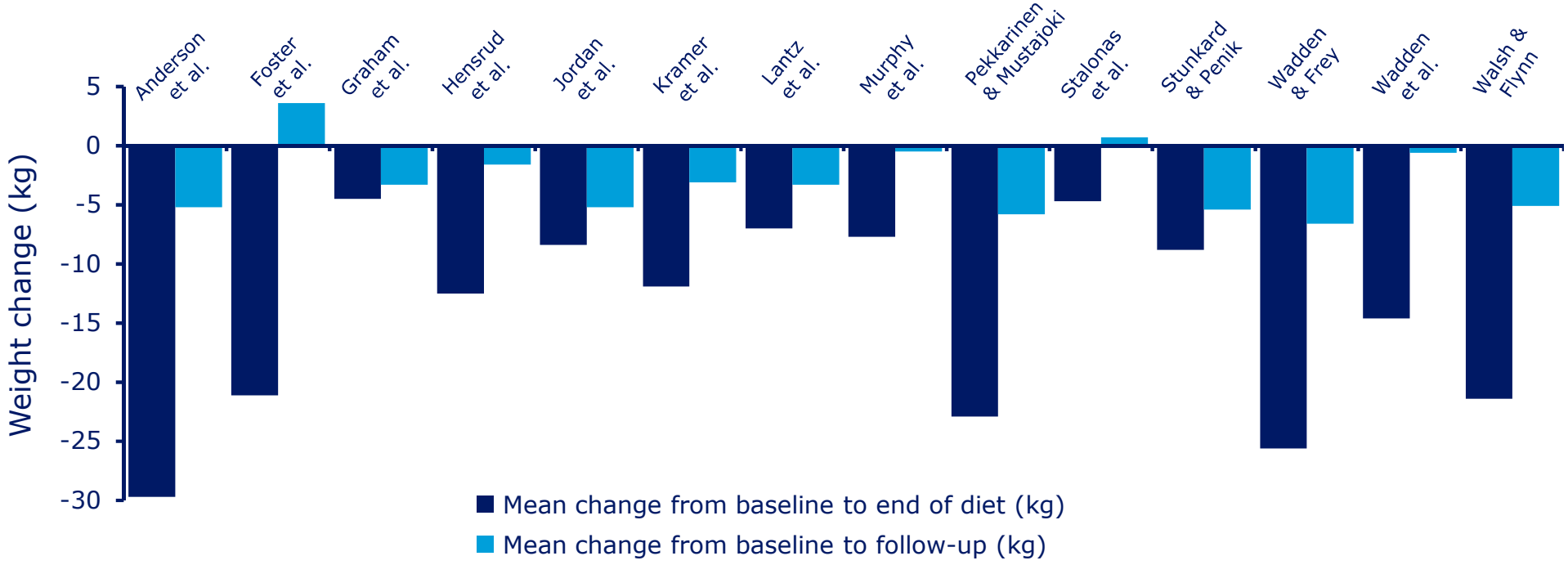
The role of the brain in controlling eating





Vallis *et al. Clin Obes* 2019;9:e12299

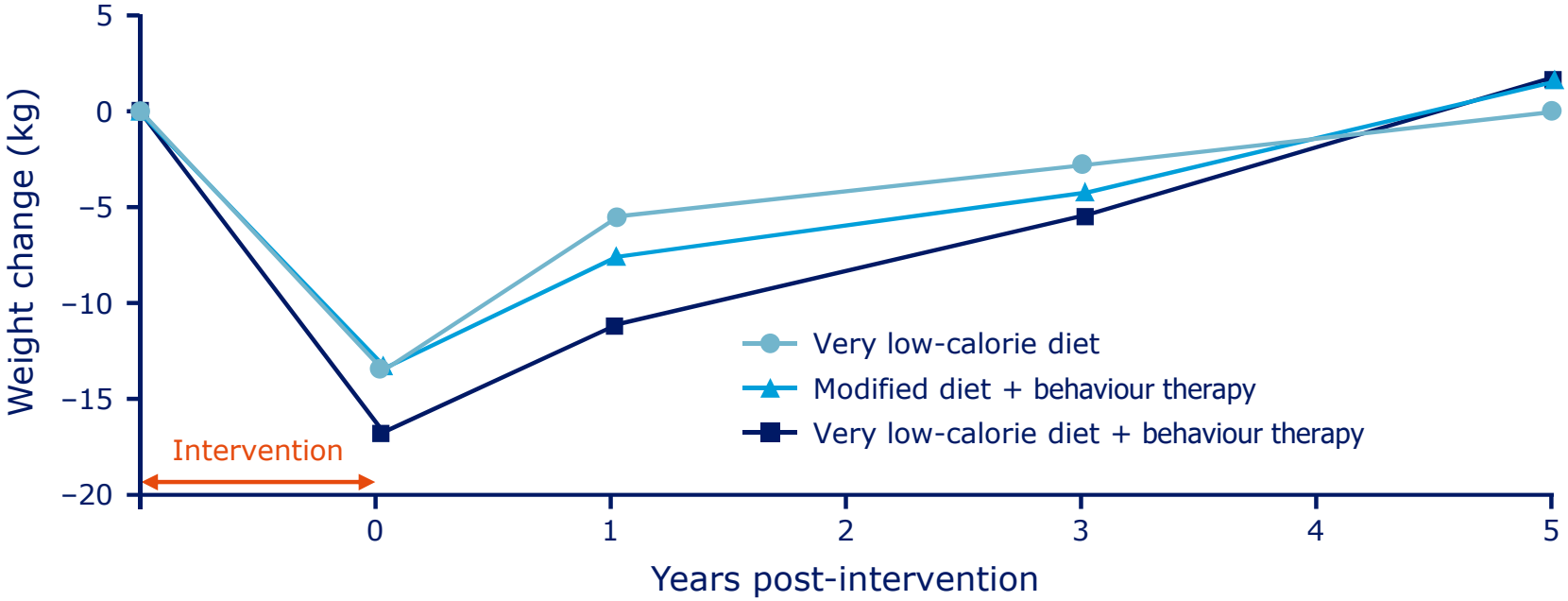
Maintenance of weight loss is challenging



Follow-up range from 4 to 7 years

Mann *et al. Am Psychol* 2007;62:220–33

Weight management interventions are often followed by weight rebound

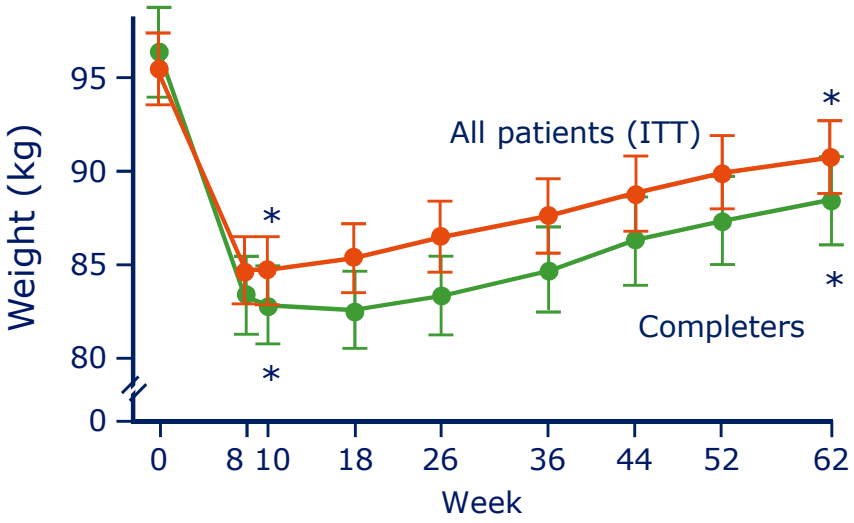


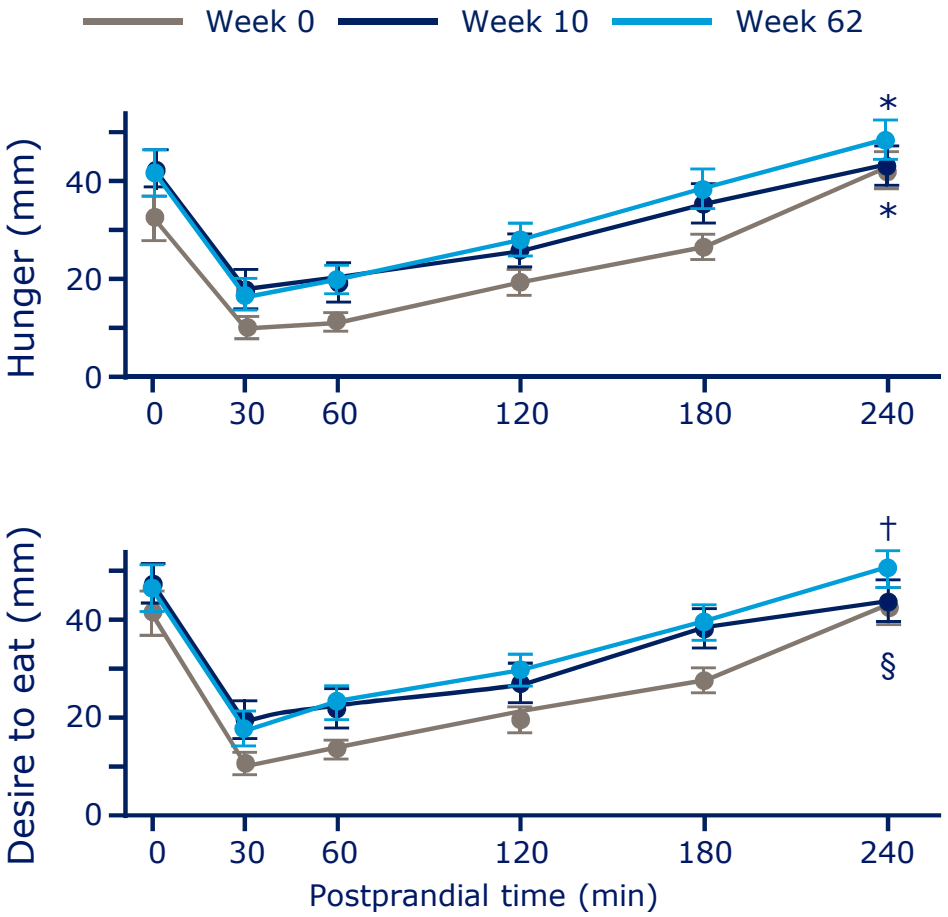
Data are from diet and behavioural interventions

Wadden *et al*. *Ann Intern Med* 1993;119:688–93

Hunger increases in response to weight loss

- 50 individuals with overweight/obesity lost weight on a 10-week VLCD
- Appetite was measured using VAS scores at 0, 10 and 62 weeks

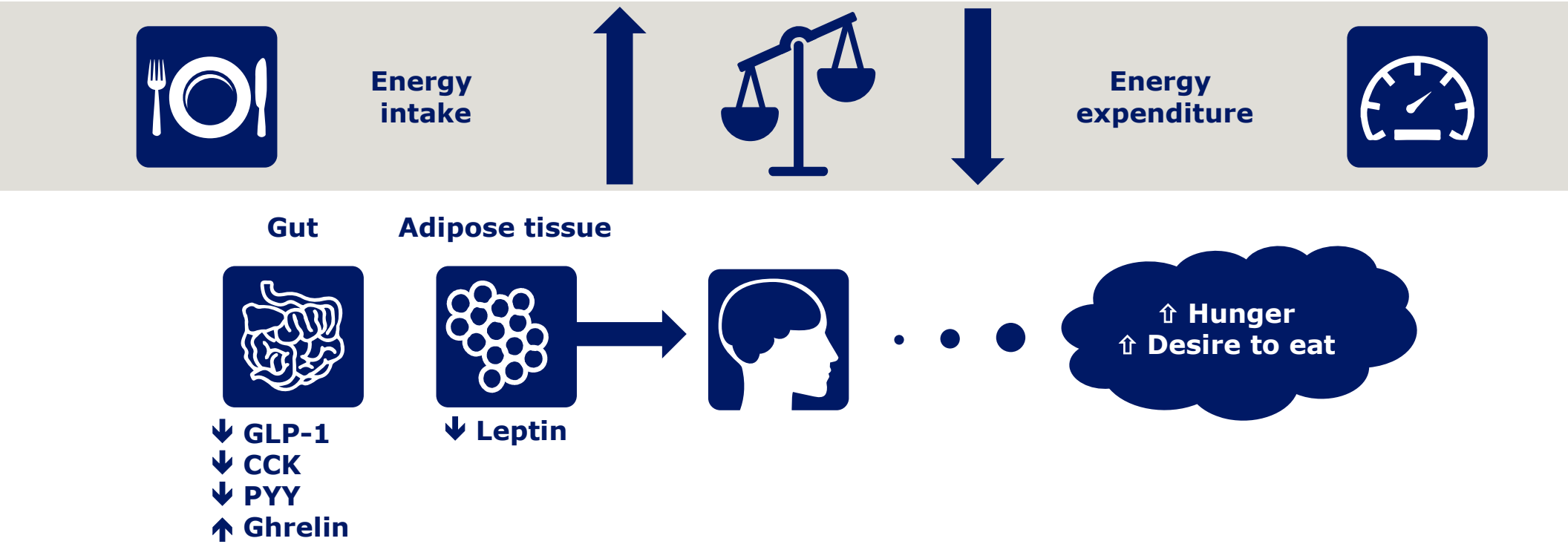




*p<0.001, §p=0.008, †p=0.09 vs mean at baseline (week 0)

Sumithran *et al. N Engl J Med* 2011;365:1597–604

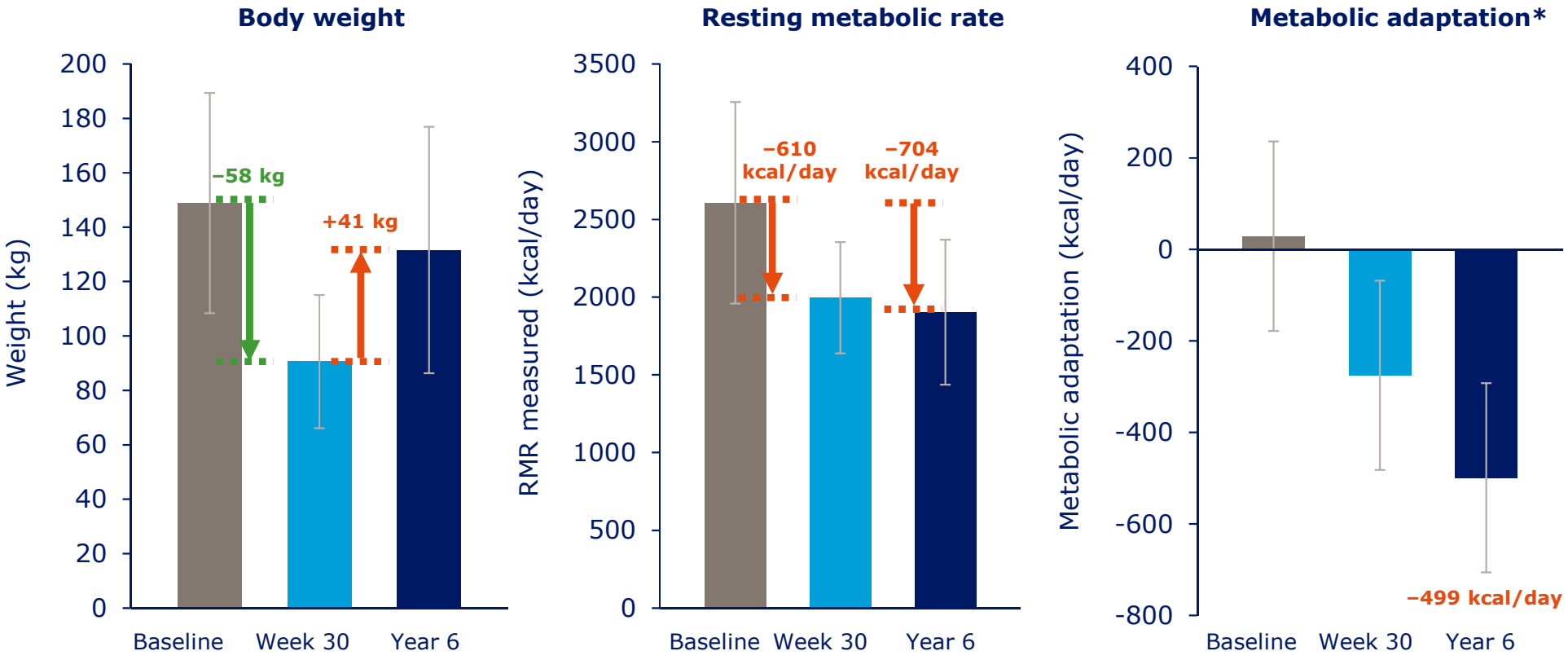
Physiological responses to weight loss favour weight regain[1,2]



CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY

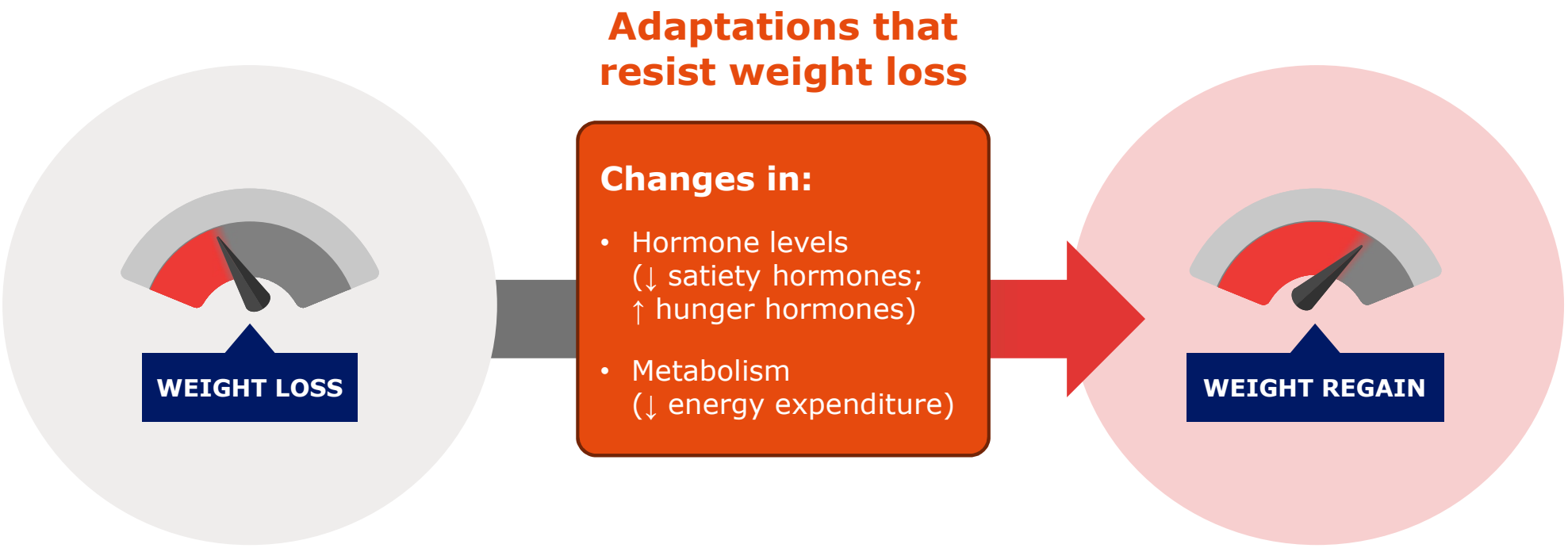
1. Schwartz *et al. Obes Rev* 2010;11:531–47; 2. Sumithran *et al. N Engl J Med* 2011;365:1597–604

Persistent metabolic adaption following weight loss



Error bars represent standard deviation. Data are for 14/16 participants in the 30-week Biggest Loser weight-loss competition.
*Defined as the residual resting metabolic rate after adjusting for changes in body composition and age.
Fothergill et al. *Obesity (Silver Spring)* 2016;24:1612–19.

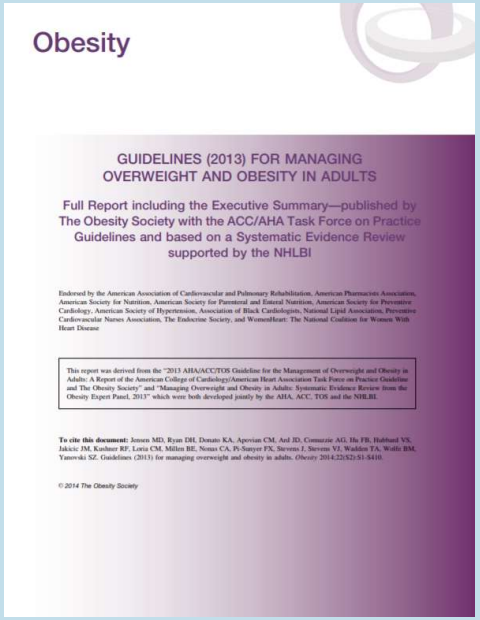
Metabolic adaptation following weight loss



Fothergill E, Guo J, Howard L, et al. Obesity (Silver Spring). 2016;24:1612– 1619. Sumithran P, Prendergast LA, Delbridge E, et al. N Engl J Med. 2011;365:1597–1604

Current obesity treatment guidelines

Obesity ACC/AHA/TOS 2014[1]


Obesity

GUIDELINES (2013) FOR MANAGING OVERWEIGHT AND OBESITY IN ADULTS

Full Report including the Executive Summary—published by The Obesity Society with the ACC/AHA Task Force on Practice Guidelines and based on a Systematic Evidence Review supported by the NHLBI

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Nutrition, American Society for Parenteral and Enteral Nutrition, American Society for Preventive Cardiology, American Society of Hypertension, Association of Black Cardiologists, National Lipid Association, Preventive Cardiovascular Nurses Association, The Endocrine Society, and WomenHeart: The National Coalition for Women With Heart Disease

This report was derived from the "2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society" and "Managing Overweight and Obesity in Adults: Systematic Evidence Review from the Obesity Expert Panel, 2013" which were both developed jointly by the AHA, ACC, TOS and the NHLBI.

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AACE Clinical Practice Guidelines 2016[2]


AACE/ACE Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY

*W. Timothy Garvey, MD, FACE[1]; Jeffrey I. Mechanick, MD, FACP, FACE, FACN, ECNU[2]; Elise M. Brett, MD, FACE, CNSC, ECNU[3]; Alan J. Garber, MD, PhD, FACE[4]; Daniel L. Hurley, MD, FACE[5]; Ania M. Jastreboff, MD, PhD[6]; Karl Nadolsky, DO[7]; Rachel Pessah-Pollack, MD[8]; Raymond Plodkowski, MD[9]; and Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines**

American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice are systematically developed statements to assist health care professionals in medical decision-making for specific clinical conditions. Most of the content herein is based on a systematic review of evidence published in peer-reviewed literature. In areas in which there was some uncertainty, professional judgment was applied.

These guidelines are a working document reflecting the state of the field at the time of publication. Because rapid changes in this area are expected, periodic revisions are inevitable. We encourage medical professionals to use this information in conjunction with their best clinical judgment. The presented recommendations may not be appropriate in all situations. Any decision by practitioners to apply these guidelines must be made in light of local resources and individual patient circumstances.

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ENDOCRINE PRACTICE Vol 22 (Suppl 3) July 2016 1

EASO Guidelines for Obesity Management 2015[3]


ObesityFacts

Obes Facts 2015;8:402–424

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Clinical Information

European Guidelines for Obesity Management in Adults

Volkan Yumuk[a] Constantine Tsigos[b] Martin Fried[c] Karin Schindler[d] Luca Busetto[e] Dragan Micic[f] Hermann Toplak[g] for the Obesity Management Task Force of the European Association for the Study of Obesity

[a]Division of Endocrinology, Metabolism and Diabetes, Department of Medicine, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [b]Department of Nutrition and Dietetics, Harokopio University, Athens, Greece; [c]Clinical Center for Minimally Invasive and Bariatric Surgery, ISCARE Lighthouse, Prague and 1st Medical Faculty, Charles University, Prague, Czech Republic; [d]Department of Medicine III, Medical University of Vienna, Vienna, Austria; [e]Department of Medicine, Padova University Hospital – Bariatric Unit, University of Padova, Padova, Italy; [f]Centre for Metabolic Disorders in Endocrinology, Institute of Endocrinology, Diabetes and Diseases of Metabolism, Clinical Center of Serbia, Belgrade, Serbia; [g]Department of Medicine, Institute for Diabetes and Metabolism, Medical University, Graz, Austria

Key Words
European guidelines · Obesity management · Multidisciplinary · Primary care · OMTF · COMs

Abstract
Obesity is a chronic metabolic disease characterised by an increase of body fat stores. It is a gateway to ill health, and it has become one of the leading causes of disability and death, affecting not only adults but also children and adolescents worldwide. In clinical practice, the body fatness is estimated by BMI, and the accumulation of intra-abdominal fat (marker for higher metabolic and cardiovascular disease risk) can be assessed by waist circumference. Complex interactions between biological, behavioural, social and environmental factors are involved in regulation of energy balance and fat stores. A comprehensive history, physical examination and laboratory assessment relevant to the patient's obesity should be obtained. Appropriate goals of weight management emphasise realistic weight loss to achieve a reduction in health risks and should include promotion of weight loss, maintenance and prevention of weight regain. Management of co-morbidities and improving quality of life of obese patients are also included in treatment aims. Balanced hypocaloric diets result in clinically meaningful weight loss regardless of which macronutrients they emphasise. Aerobic training is the optimal mode of exercise for reducing fat mass while a programme including resistance train-

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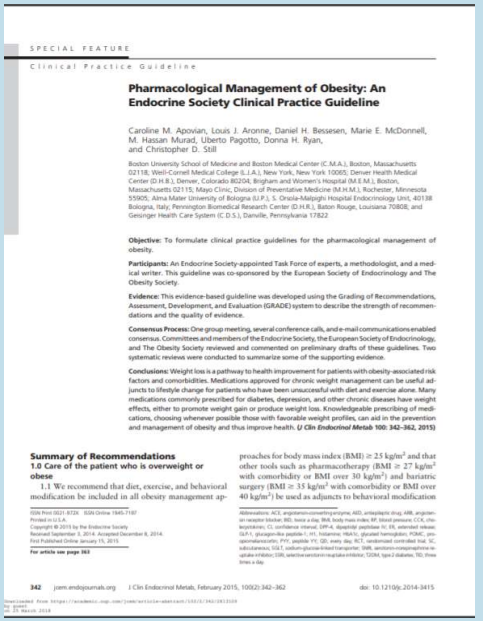
KARGER 125

ENDO Pharma Management 2015[4]


SPECIAL FEATURE

Clinical Practice Guideline

Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline

Caroline M. Apovian, Louis J. Aronne, Daniel H. Bessesen, Marie E. McDonnell, M. Hassan Murad, Uberto Pagotto, Donna H. Ryan, and Christopher D. Still

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Objective: To formulate clinical practice guidelines for the pharmacological management of obesity.

Participants: An Endocrine Society-appointed Task Force of experts, a methodologist, and a medical writer. This guideline was co-sponsored by the European Society of Endocrinology and The Obesity Society.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe the strength of recommendations and the quality of evidence.

Consensus Process: One group meeting, several conference calls, and e-mail communications enabled consensus. Committees and members of the Endocrine Society, the European Society of Endocrinology, and The Obesity Society reviewed and commented on preliminary drafts of these guidelines. Two systematic reviews were conducted to summarize some of the supporting evidence.

Conclusions: Weight loss is a pathway to health improvement for patients with obesity-associated risk factors and comorbidities. Medications approved for chronic weight management can be useful adjuncts to lifestyle change for patients who have been unsuccessful with diet and exercise alone. Many medications commonly prescribed for diabetes, depression, and other chronic diseases have weight effects, either to promote weight gain or produce weight loss. Knowledgeable prescribing of medications, choosing whenever possible those with favorable weight profiles, can aid in the prevention and management of obesity and thus improve health. *(J Clin Endocrinol Metab* 100: 342–362, 2015)

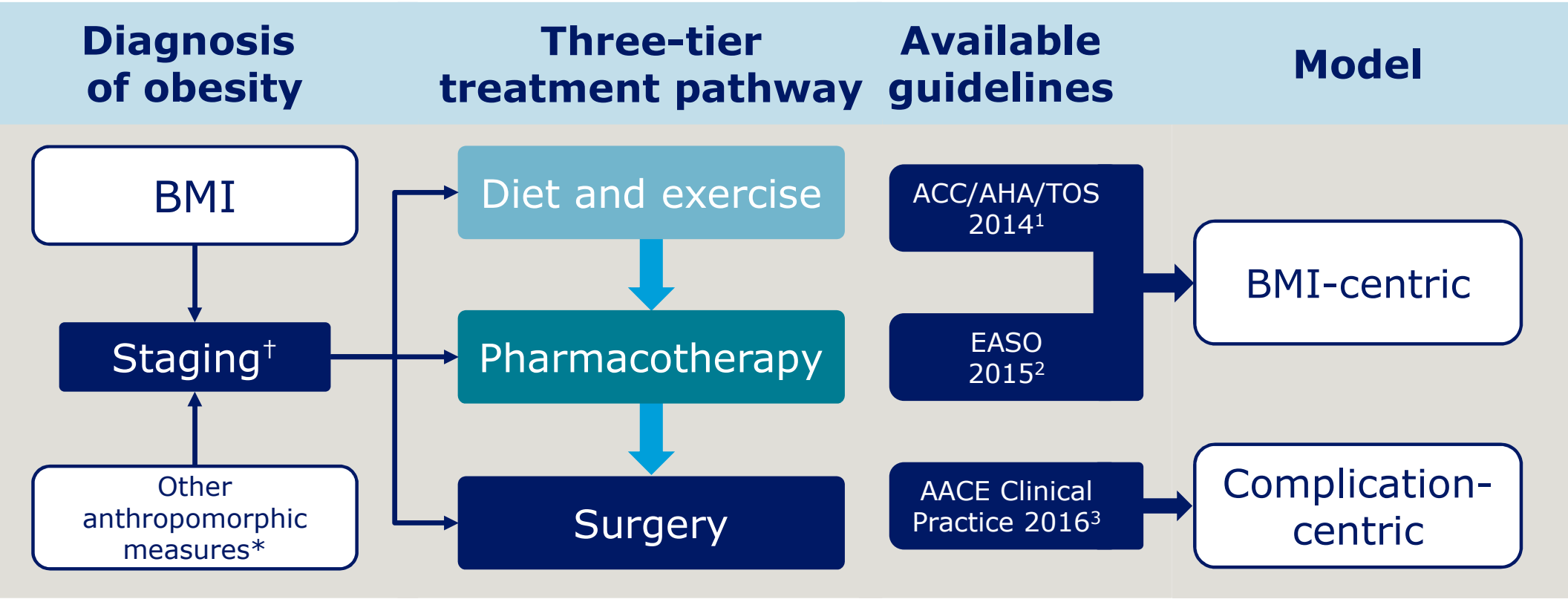
Summary of Recommendations

1.0 Care of the patient who is overweight or obese

1.1 We recommend that diet, exercise, and behavioral modification be included in all obesity management approaches for body mass index (BMI) ≥ 25 kg/m² and that other tools such as pharmacotherapy (BMI ≥ 27 kg/m² with comorbidity or BMI over 30 kg/m²) and bariatric surgery (BMI ≥ 35 kg/m² with comorbidity or BMI over 40 kg/m²) be used as adjuncts to behavioral modification

1. Jensen *et al*. *Circulation* 2014;129(25 Suppl 2):S102–38; 2. Garvey *et al*. *Endocr Pract* 2016;22(Suppl 3):1–203; 3. Yumuk *et al. Obes Facts* 2015;8:402–424;
4. Apovian *et al*. *J Clin Endocrinol Metab* 2015;100:342–62

Guidelines describe obesity treatment pathway



*Other measures include waist circumference and body composition assessments. †Optional step

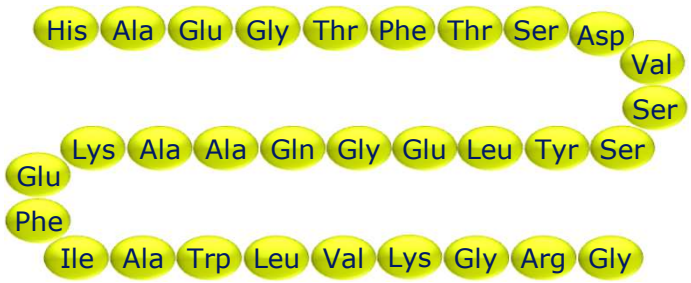
1. Jensen *et al*. *Circulation* 2014;129(25 Suppl 2):S102–38; 2. Yumuk *et al. Obes Facts* 2015;8:402–424; 3. Garvey *et al*. *Endocr Pract* 2016;22(Suppl 3):1–203

Pharmacological options for weight management

				Mode of action	Indications
Orlistat	✓	✓	✓	Energy wastage	Adjunct to diet and physical activity for chronic weight management in a) obesity BMI ≥30 kg/m^2 b) overweight BMI ≥27 kg/m^2 with comorbidity
Phentermine*	✗	✓	✓	Appetite suppression	
Phentermine/topiramate	✗	✓	✗	Appetite suppression	
Lorcaserin	✗	✗	✗	Appetite suppression	
Naltrexone/bupropion	✓	✓	✗	Appetite suppression	
Liraglutide 3.0 mg	✓	✓	✓	Appetite suppression	
Sibutramine	✗	✗	✗	Appetite suppression	n/a

*Approved for short-term use. FDA Drugs: http://www.fda.gov/Drugs/default.htm; EMA Medicines: http://www.ema.europa.eu/

Liraglutide is a once-daily, human GLP-1 analogue



Human endogenous GLP-1

$T_{½}$= ~2 mins

C-16 fatty acid (palmitoyl)

Liraglutide

97% amino acid homology to human GLP-1; improved PK: albumin binding through acylation; heptamer formation

↓

Slow absorption from subcutis
Resistant to DPP-4
Long plasma half-life
($T_{½}$=13 h)

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; PK, pharmacokinetics; $T_{½}$, plasma half-life

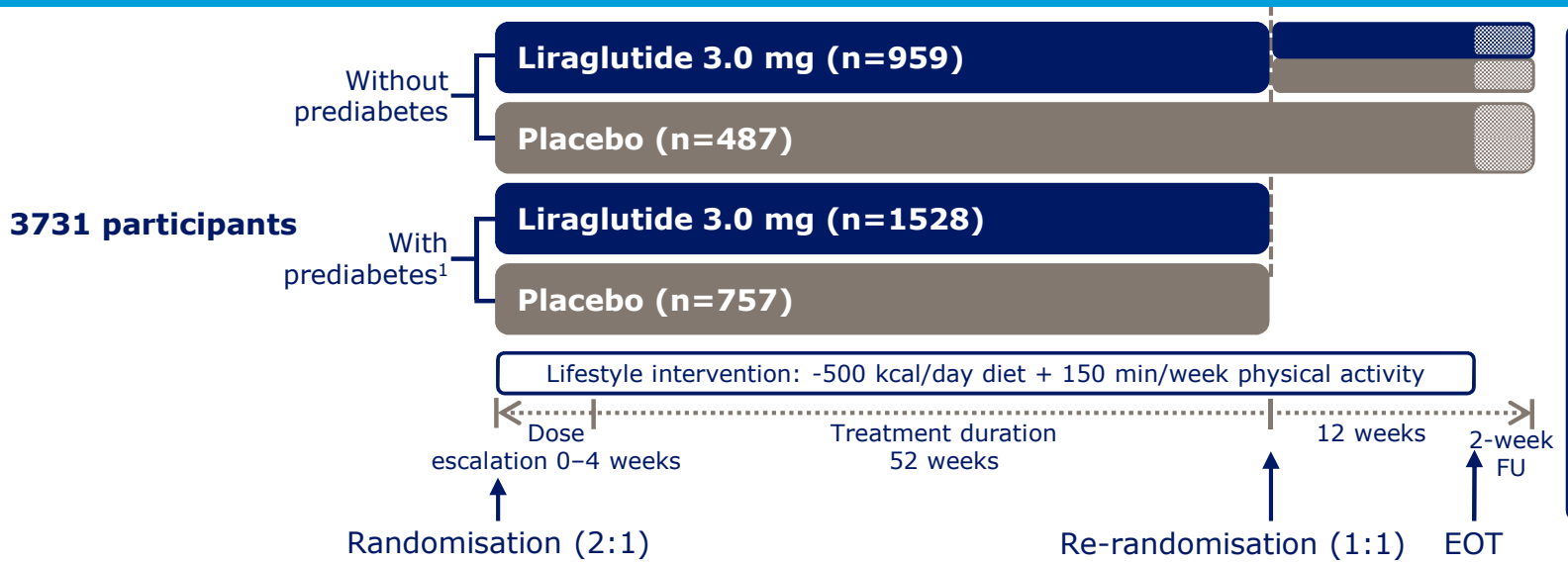
Knudsen *et al. J Med Chem* 2000;43:1664–9; Degn *et al. Diabetes* 2004;53:1187–94

Trial design: SCALE Obesity and Prediabetes

Liraglutide 3.0 mg in weight management (56 weeks)

Trial objective

Efficacy and safety of liraglutide 3.0 mg, as adjunct to D&E, in participants with obesity or overweight plus comorbidities, without diabetes



Trial information

- June 2011 to March 2013
- Randomised controlled double-blind study
- 191 sites in 27 countries
- Duration: 56 weeks (with prediabetes), 68 weeks (without prediabetes)

1. ADA. *Diabetes Care* 2010;33(Suppl. 1):S11–61

BW, body weight; D&E, diet and exercise; EOT, end of treatment; FU, follow-up; HRQoL, health-related quality of life; WC, waist circumference

Pi-Sunyer *et al*. *N Engl J Med* 2015;373:11–22

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Liraglutide 3.0 mg in weight management (56 weeks)

Inclusion criteria

- ≥18 years
- Stable BW
- BMI ≥30 kg/m^2
  or
  ≥27 kg/m^2 + comorbidities

Key endpoints

- Three co-primary: BW change, 5% or 10% BW loss
- Secondary: Changes from baseline in BMI, WC, glycaemic control variables, cardiometabolic risk factors, and HRQoL

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Baseline characteristics

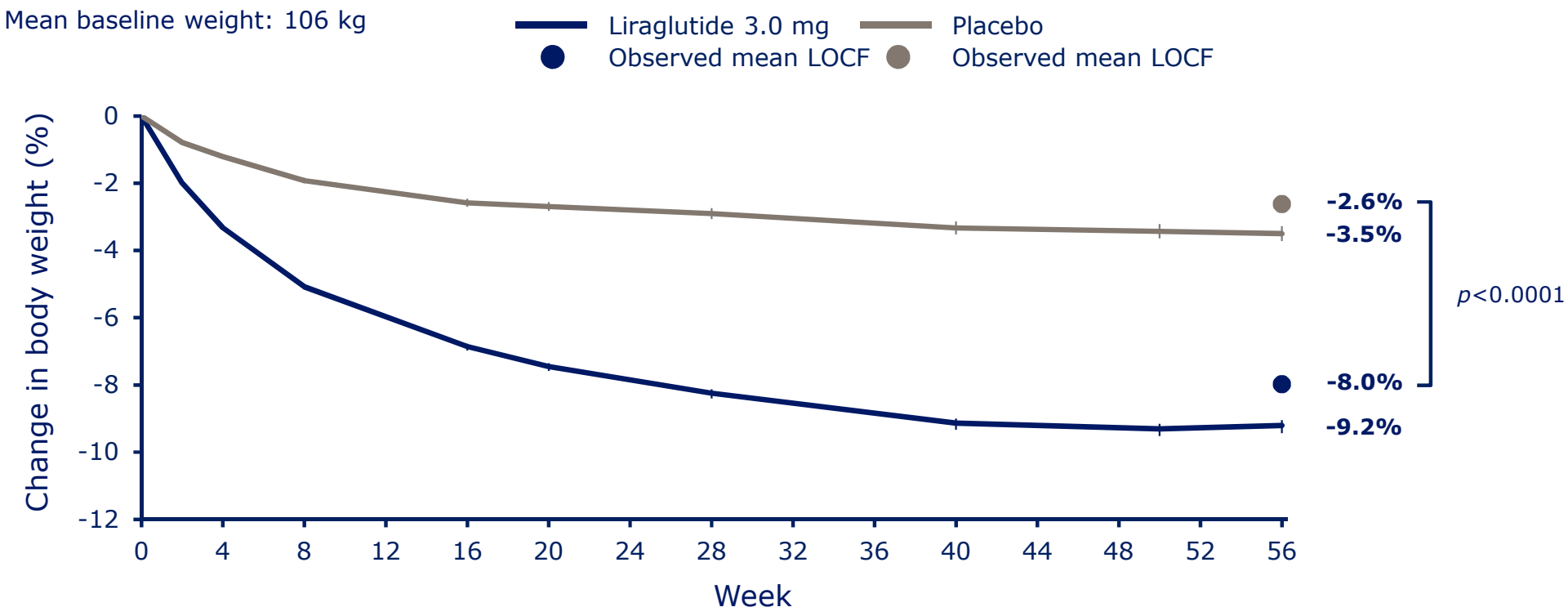
	Without prediabetes[§]				With prediabetes			
	Liraglutide 3.0 mg		Placebo		Liraglutide 3.0 mg		Placebo	
	n	(%)	n	(%)	n	(%)	n	(%)
Number of subjects	959	(100.0)	487	(100.0)	1528	(100.0)	757	(100.0)
Female	801	(83.5)	390	(80.1)	1156	(75.7)	581	(76.8)
Race – White - no. (%)[†]	831	(86.7)	426	(87.5)	1276	(83.5)	635	(83.9)
Mean age (years)	41.6		41.5		47.4		47.2	
Mean body weight (kg)	104.0		103.6		107.6		107.9	
Mean BMI[‡] (kg/m^2)	37.5		37.4		38.8		39.0	
≤29.9	27	(2.8)	21	(4.3)	39	(2.6)	23	(3.0)
30.0–34.9 – Obese class I	372	(38.8)	190	(39.0)	434	(28.4)	198	(26.2)
35.0–39.9 – Obese class II	288	(30.0)	147	(30.2)	499	(32.7)	251	(33.2)
≥40.0 – Obese class III	272	(28.4)	129	(26.5)	556	(36.4)	285	(37.6)
Hypertension[¶]	211	(22.0)	130	(26.7)	639	(41.8)	316	(41.7)
Dyslipidaemia[¶]	233	(24.3)	113	(23.2)	504	(33.0)	246	(32.5)

All subjects randomised. BMI, body mass index. §Prediabetes was defined according to ADA 2010 criteria. †Race and ethnic group were self-reported. ‡The body-mass index is the weight in kilograms divided by the square of the height in meters. ¶Dyslipidemia and hypertension were based on reported medical history

Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

Change in body weight (%)

0–56 weeks



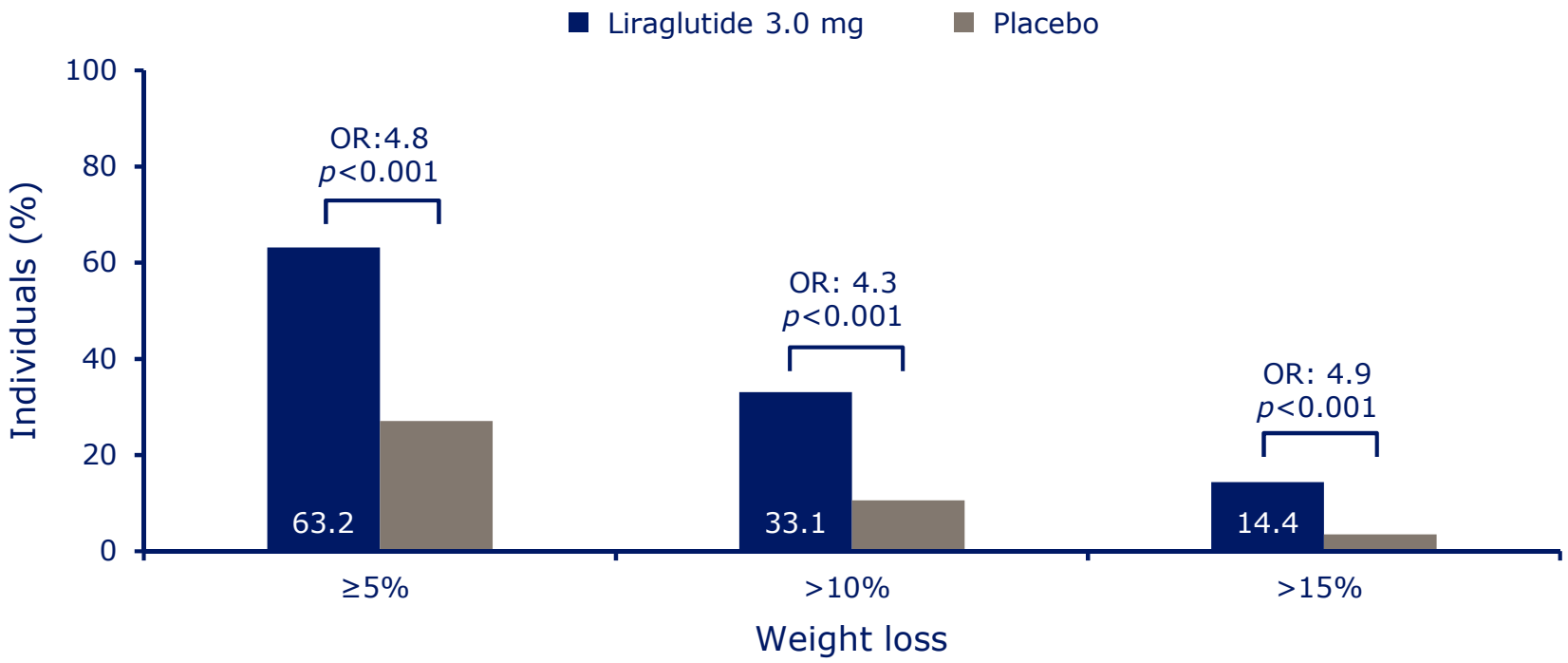
FAS, fasting visit data only. Line graphs are observed means (±SE). Statistical analysis is ANCOVA.
FAS, full analysis set; LOCF, last observation carried forward; SE, standard error

Pi-Sunyer *et al. Diabetologia* 2014;57(Suppl. 1): Abstract 73-OR

Categorical weight loss

At week 56

Mean baseline weight: 106.2 kg



Data are observed means for the full analysis set (with LOCF) and the odds ratios (OR) shown are from a logistic regression analysis (the analysis for achieving 15% weight loss was performed post hoc). LOCF, last observation carried forward; OR, odds ratio

Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

SCALE Obesity and Prediabetes

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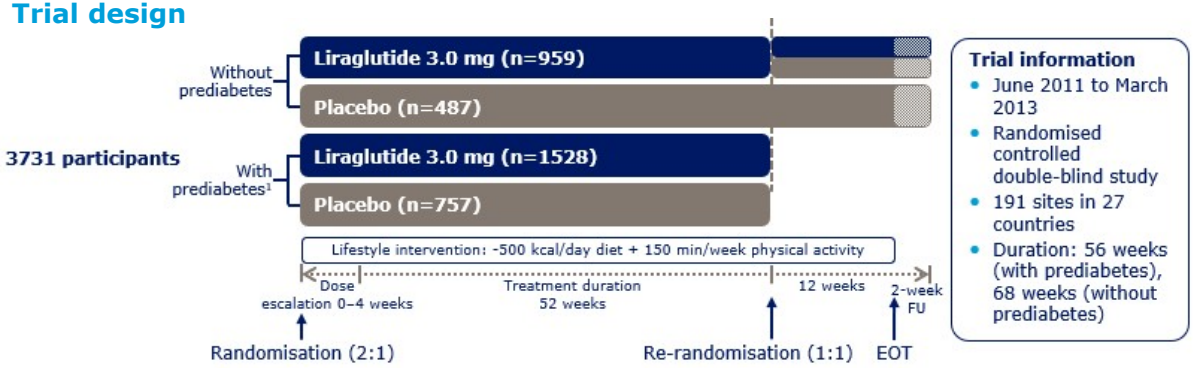
Aim (56 weeks) Efficacy and safety of liraglutide 3.0 mg, as adjunct to D&E, in participants with obesity or overweight plus comorbidities, without diabetes

Trial design



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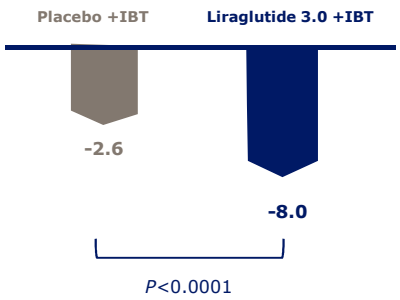
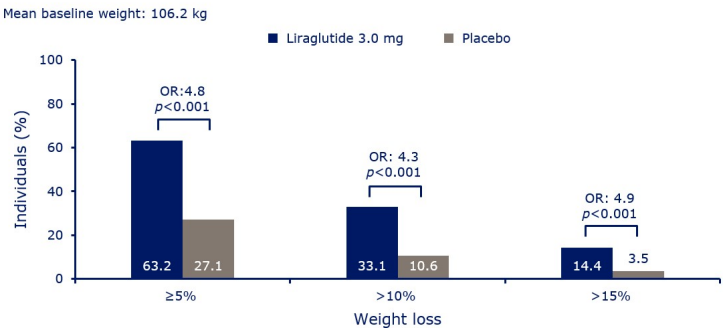
Key findings (56 weeks)

Change in body weight (%)



Individuals achieving ≥5, >10, or >15% categorical weight loss



Key secondary endpoints (56 weeks)

Waist circumference (cm)	**-8.2 vs -3.9, p<0.001**
HbA_{1c} (%)	**-0.30 vs -0.06, p<0.001**
FPG (mg/dL)	**-7.1 vs 0.1, p<0.001**
Cardiometabolic variables & HRQoL	Beneficial effects with liraglutide for blood pressure and other cardiometabolic variables and with improvement in HRQoL
Safety	Safety profile was generally consistent with that of previous clinical trials with liraglutide 3.0 mg and liraglutide 1.8 mg in individuals with T2D

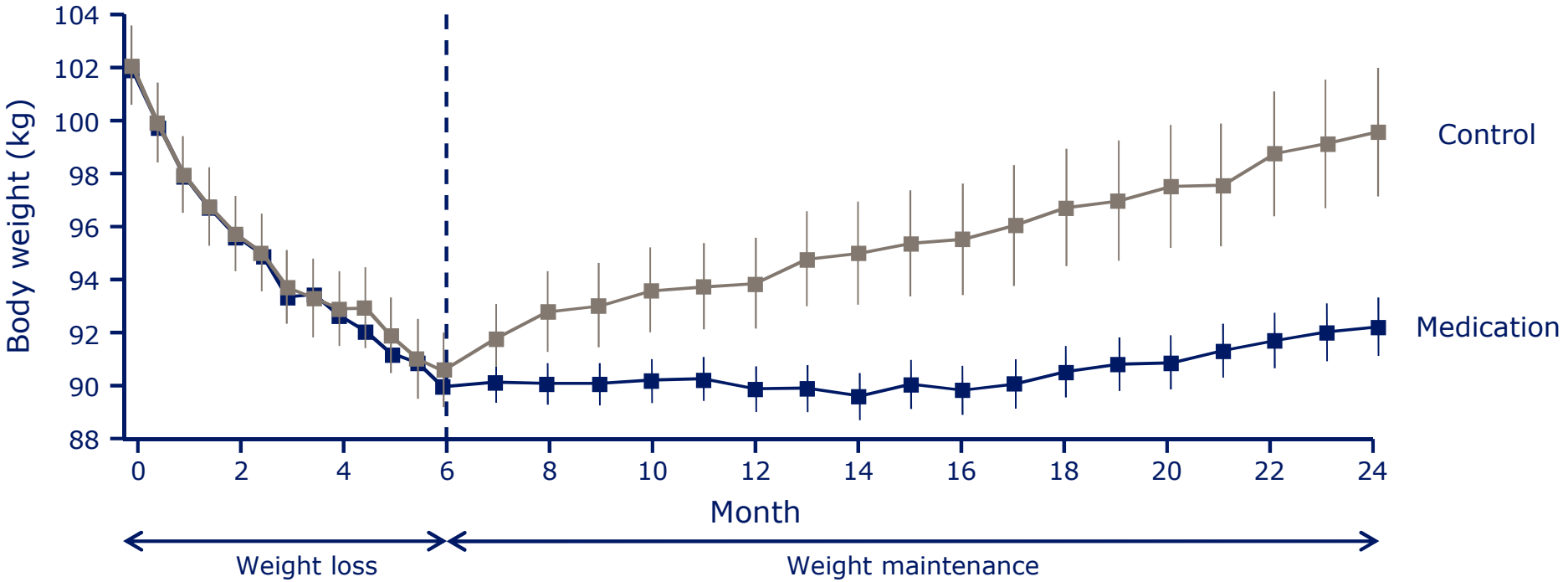
Conclusion

Liraglutide, as an adjunct to diet and exercise, was associated with reduced body weight and improved metabolic control.

BW, body weight; D&E, diet and exercise; EOT, end of treatment; FU, follow-up; HRQoL, health-related quality of life; WC, waist circumference

Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

A long-term approach to obesity management is required for maintaining weight loss



James *et al. Lancet* 2000;356:2119–25

EMA stopping rule for anti-obesity medications

Regulatory requirement

Weight loss target: ≥5% at week 12*

Wording: Treatment with Saxenda® should be discontinued after ***12 weeks on the 3.0 mg/day*** dose if patients have not lost ***at least 5%*** of their initial body weight

Weight loss target: ≥4% at week 16

Wording: Evaluate the change in body weight ***16 weeks*** after initiating Saxenda® and discontinue Saxenda® if the patient has not lost ***at least 4%*** of baseline body weight

*Corresponds to approximately 16 weeks of treatment when including the dose titration period
EMA, European Medicines Agency

Novo Nordisk. Saxenda® SmPC 2015. Available at: http://ec.europa.eu/health/documents/community-register/2015/20150323131125/anx_131125_en.pdf