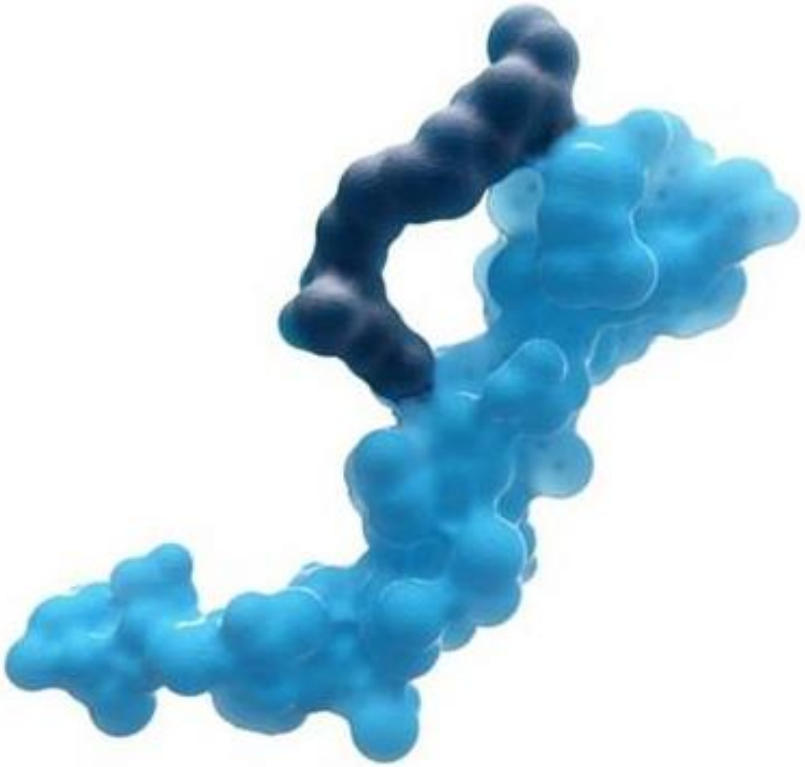

The role of GLP-1 in weight management

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Vice President
Obesity, NASH & Publications
Global Medical Affairs
Novo Nordisk A/S

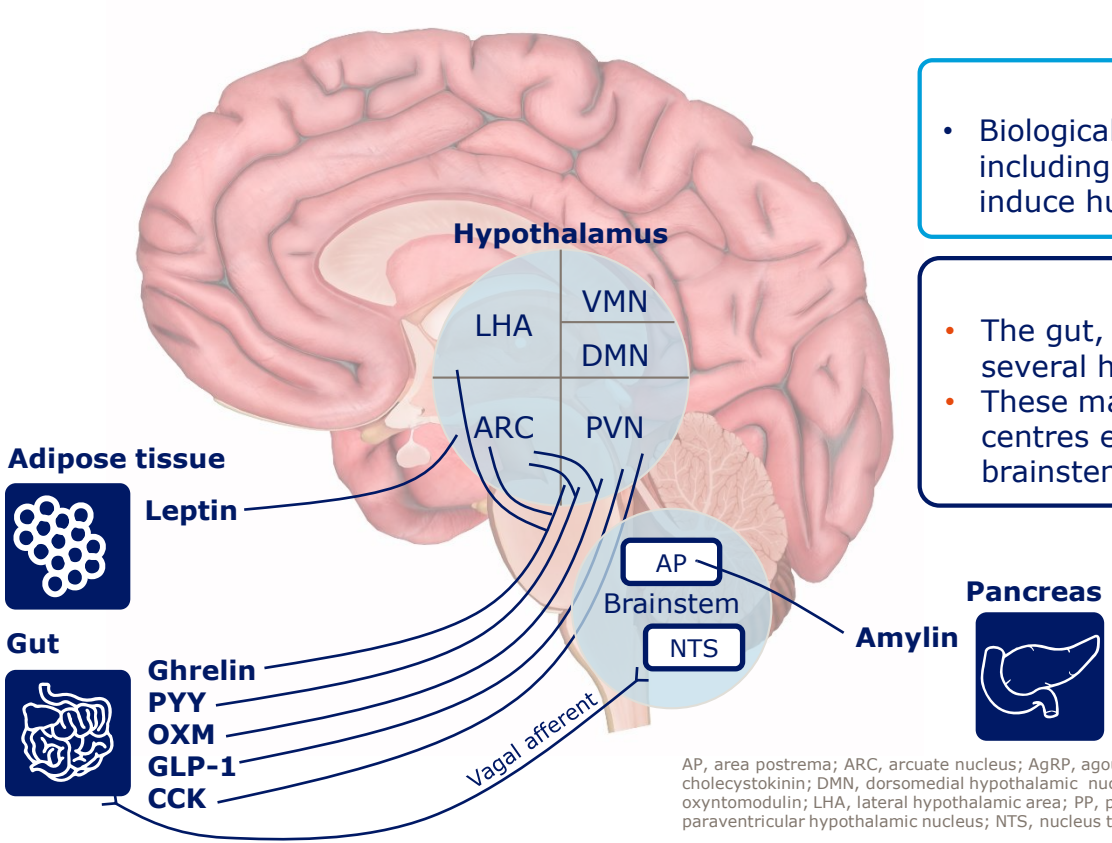
Conflicts of interest

- I’m an employee of Novo Nordisk A/S
- I’m a shareholder in Novo Nordisk A/S

Session outline

- Homeostatic and hedonic appetite regulation
- GLP-1 physiology
- GLP-1 effects on appetite regulation
- Liraglutide, a human GLP-1 analogue
- Liraglutide effects on appetite regulation and body weight
- Liraglutide in weight management
- Clinical perspectives

Homeostatic regulation of appetite



Homeostatic regulation

- Biological systems act to maintain body weight, including regulation via peptide hormones that can induce hunger/satiety

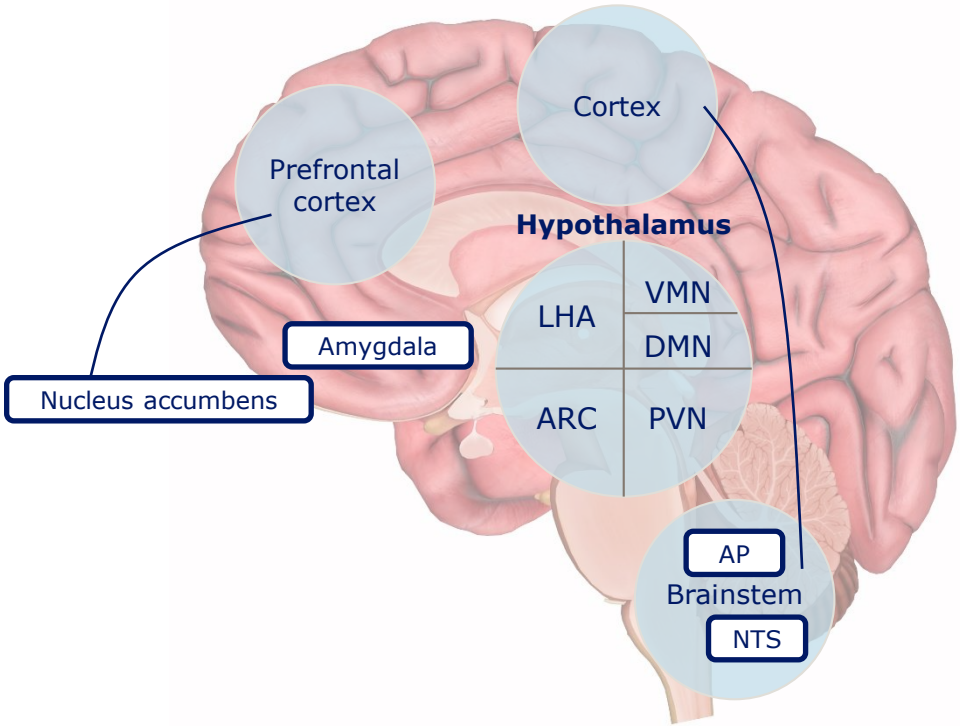
Gut hormone system

- The gut, adipose tissue and pancreas produce several hormones that promote satiety or hunger
- These may influence central appetite control centres either directly via vagal afferents and the brainstem

AP, area postrema; ARC, arcuate nucleus; AgRP, agouti-related peptide; CART, cocaine and amphetamine regulated transcript; CCK, cholecystokinin; DMN, dorsomedial hypothalamic nucleus; GLP-1, glucagon-like peptide-1; NPY, neuropeptide Y; OXM, oxyntomodulin; LHA, lateral hypothalamic area; PP, pancreatic polypeptide; PYY, peptide-YY; POMC, pro-opiomelanocortin; PVN, paraventricular hypothalamic nucleus; NTS, nucleus tractus solitarius; VMN, ventromedial hypothalamic nucleus

Simpson *et al. Expert Rev Endocrinol Metab* 2008;3:577–92; Cooke, Bloom. *Nat Rev Drug Discov* 2006;5:919–31; Berthoud. *Curr Opin Neurobiol* 2011;21:888–96

Hedonic regulation of appetite



Hedonic regulation

- Reward of survival behaviours through pleasure
- Operates even in the presence of satiety signals
- Leads to food consumption beyond homeostatic need
- Link between hedonic attraction to food and obesity

Hedonic control systems

- Appetite is influenced by homeostatic (metabolic) and hedonic (pleasure, emotional) factors
- Hedonic appetite systems comprise external sensory information processing, reward processing, and cognition and executive functions
- Multiple different areas are involved including the amygdala and the cortex

AP, area postrema; ARC, arcuate nucleus; DMN, dorsomedial hypothalamic; LHA, lateral hypothalamic area; PVN, paraventricular hypothalamic nucleus; NTS, nucleus tractus solitarius; VMN, ventromedial hypothalamic nucleus

Simpson *et al. Expert Rev Endocrinol Metab* 2008;3:577–92; Cooke, Bloom. *Nat Rev Drug Discov* 2006;5:919–31; Berthoud. *Curr Opin Neurobiol* 2011;21:888–96

What is GLP-1?

- GLP-1 is a peptide comprised of 31 amino acids
- Member of incretin family
- Secreted predominantly from L-cells in the gut, but also the brain (nucleus tractus solitarius)

Human endogenous GLP-1

Enzymatic degradation by DPP-4

$t_{½}$=1.5–2 min

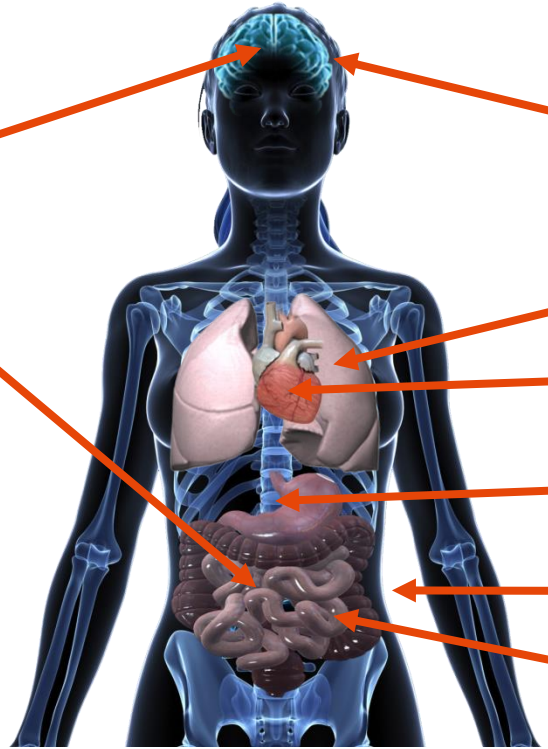
DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; $t_{½}$, half-life

Merchenthaler *et al. J Comp Neurol* 1999;403:261–80; Baggio, Drucker. *Gastroenterology* 2007;132:2131–57; Ducker, Nauck. *Lancet* 2006;368:1696–705

GLP-1 secretion and receptor expression

GLP-1 is secreted by:

- Neurons in hindbrain
- L-cells of the gut



GLP-1R is expressed in:

- Brain
- Lung
- Heart (AV node)
- Pancreas
- Kidney
- GI tract

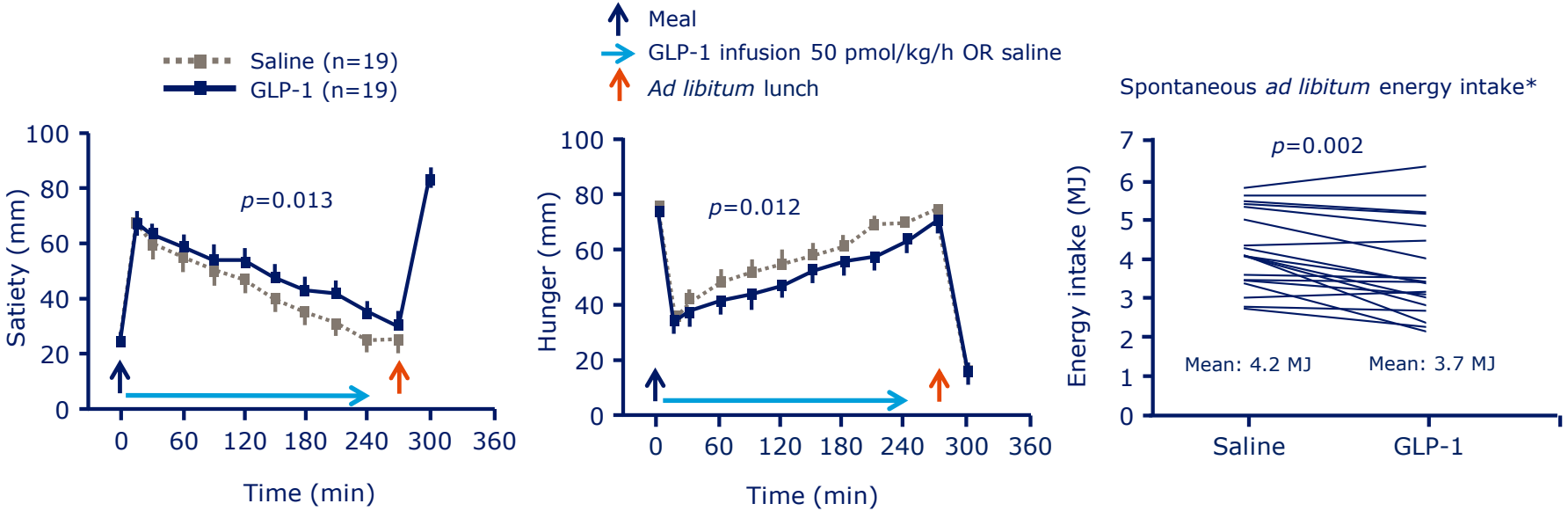
AV, atrioventricular; GI, gastrointestinal; GLP-1R, glucagon-like peptide-1 receptor

Merchenthaler *et al. J Comp Neurol* 1999;403:261–80; Baggio, Drucker. *Gastroenterology* 2007;132:2131–57; Ban *et al. Circulation* 2008;117:2340–50; Vrang *et al. Prog Neurobiol* 2010;92:442–62; Pyke *et al. Endocrinology* 2014;155:1280–90

GLP-1 increases satiety and reduces hunger

In normal weight subjects

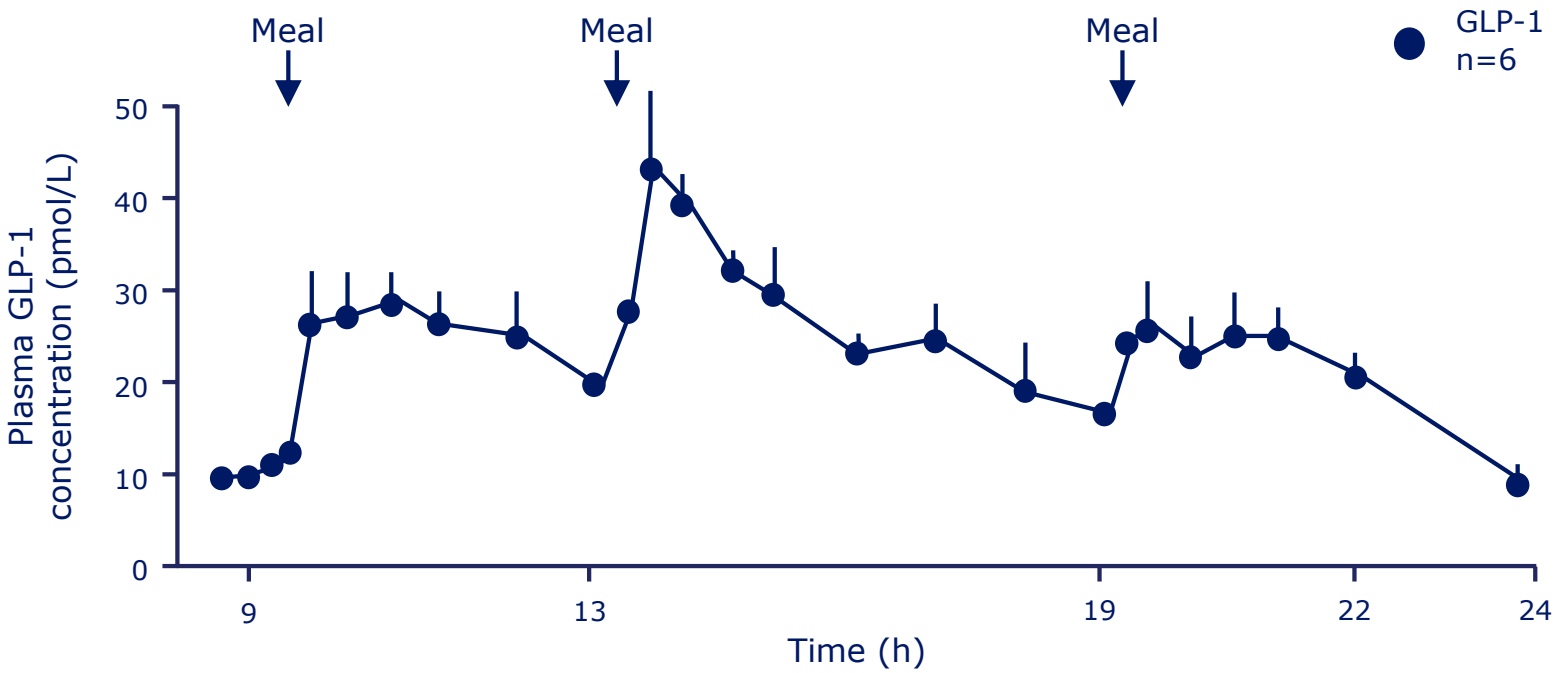
- Infusion increased plasma GLP-1 from 10 pmol/L to 60–90 pmol/L



*At an *ad libitum* lunch during GLP-1 or saline infusion in 19 healthy normal-weight male subjects. Data are mean ± SEM. GLP-1, glucagon-like peptide-1; SEM, standard error of mean

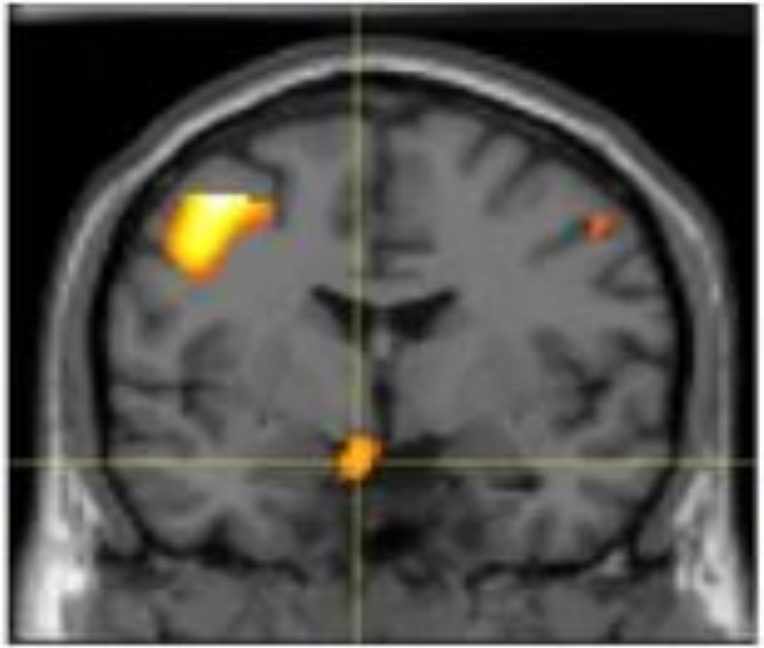
Adapted from: Flint *et al. J Clin Invest* 1998;101:515–20

GLP-1 is released in response to food intake



Adapted from: Orskov *et al. Scand J Gastroenterol* 1996;31:665–70

GLP-1 activates areas of brain involved in appetite regulation



- The postprandial GLP-1 response is associated with activation of areas of the human implicated in regulation of appetite and food intake
- Peak postprandial increases in plasma GLP-1 concentrations are correlated with increases in regional cerebral blood flow in the left dorsolateral prefrontal cortex and the hypothalamus

GLP-1, glucagon-like peptide-1; PET, positron emission tomography

Pannacciulli *et al. Neuroimage* 2007;35:511–17

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

Human endogenous GLP-1

$T_{½}$= ~2 mins

Liraglutide

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

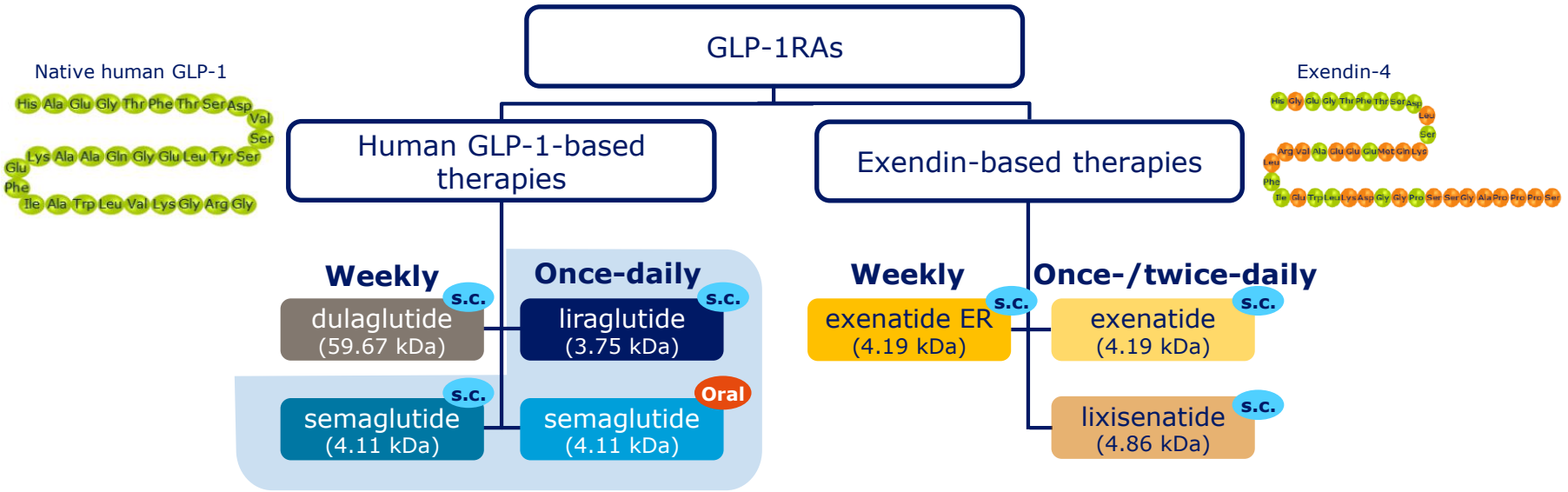
↓

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

GLP-1RAs vary in molecular structure and size



ER, extended release; GLP-1, glucagon-like peptide-1; GLP-1RA, glucagon-like peptide-1 receptor agonist; s.c., subcutaneous.

1. Wick A, Newlin K. *J Am Acad Nurse Pract*. 2009;21:623–630; 2. White J. *J Am Pharm Assoc.* 2009;49(Suppl. 1):S30–40; 3. Madsbad S et al. *Diabetes Obes Metab*. 2011;13:394–407.

GLP-1RAs have multifactorial effects

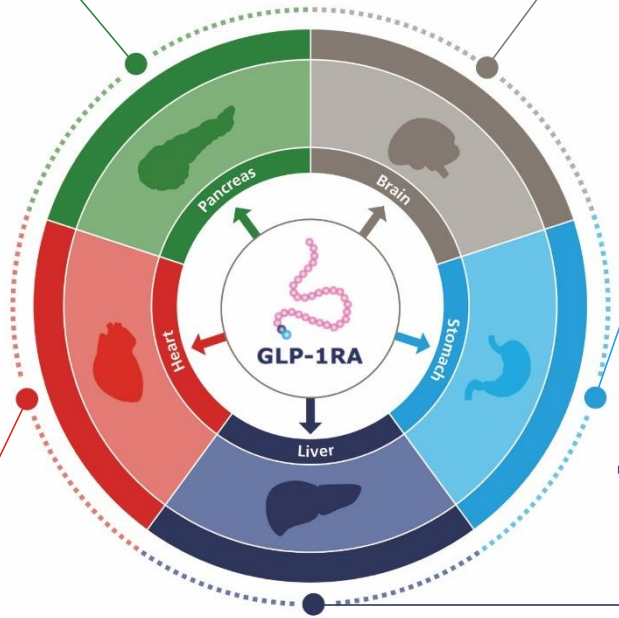
Pharmacological effects of GLP-1RAs

Pancreas

- ↑ Beta-cell function[1]
- ↓ Beta-cell apoptosis[1]
- ↑ Insulin biosynthesis[1]
- ↑ Glucose-dependent insulin secretion[1]
- ↓ Glucose-dependent glucagon secretion[1]

Brain

- ↓ Body weight[5]
- ↓ Food intake[6]
- ↑ Satiety[7,8]



Stomach

- ↓ Gastric emptying[9]

Heart

- ↓ Cardiovascular risk[2]
- ↓ Fatty acid metabolism[3]
- ↑ Cardiac function[3]
- ↓ Systolic blood pressure[3]
- ↓ Inflammation[4]

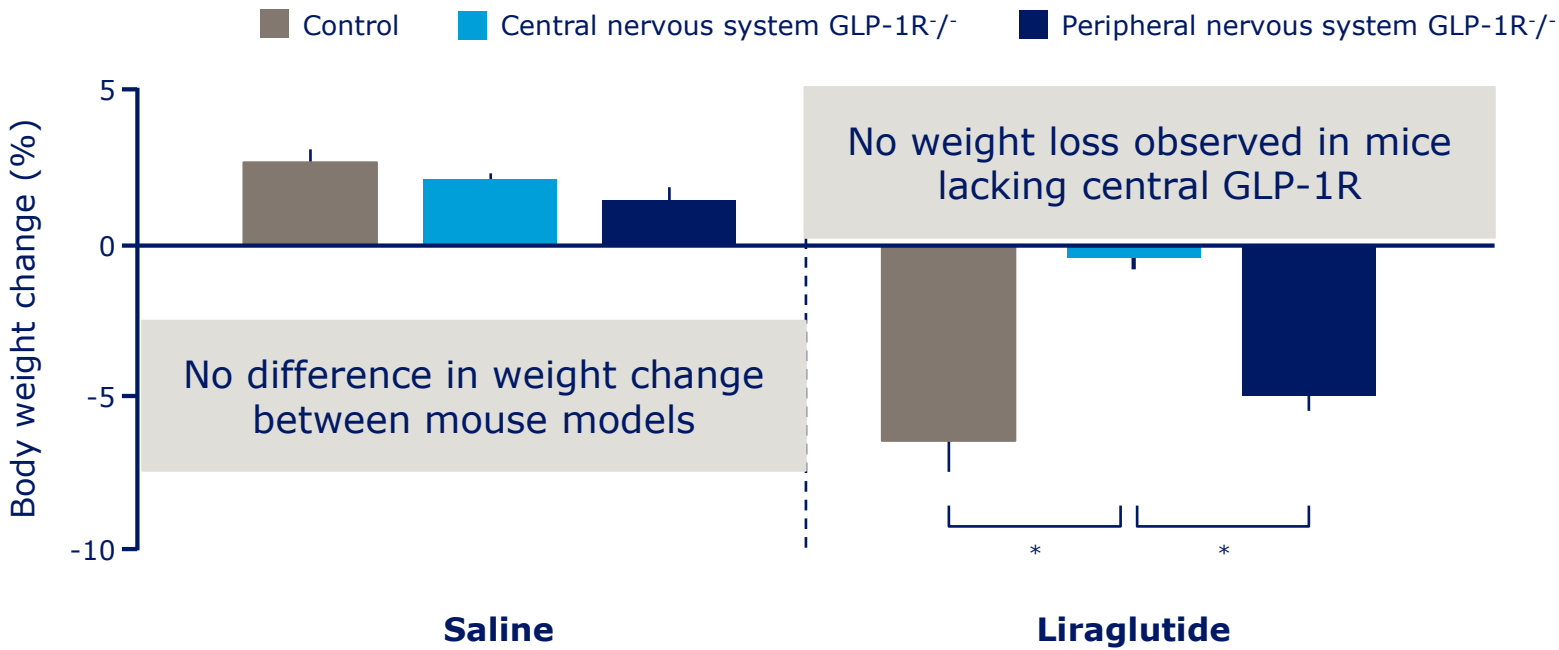
Liver

- ↓ Endogenous glucose production[10]
- ↑ Hepatic insulin sensitivity[10]
- ↓ *De novo* lipogenesis[10]
- ↓ Lipotoxicity[10]
- ↓ Steatosis[11]

GLP-1RA, glucagon-like peptide-1 receptor agonist

Adapted from Campbell & Drucker. *Cell Metab* 2013;17:819–37; Pratley & Gilbert. *Rev Diabet* Stud 2008;5:73–94. Full reference list in slide notes.

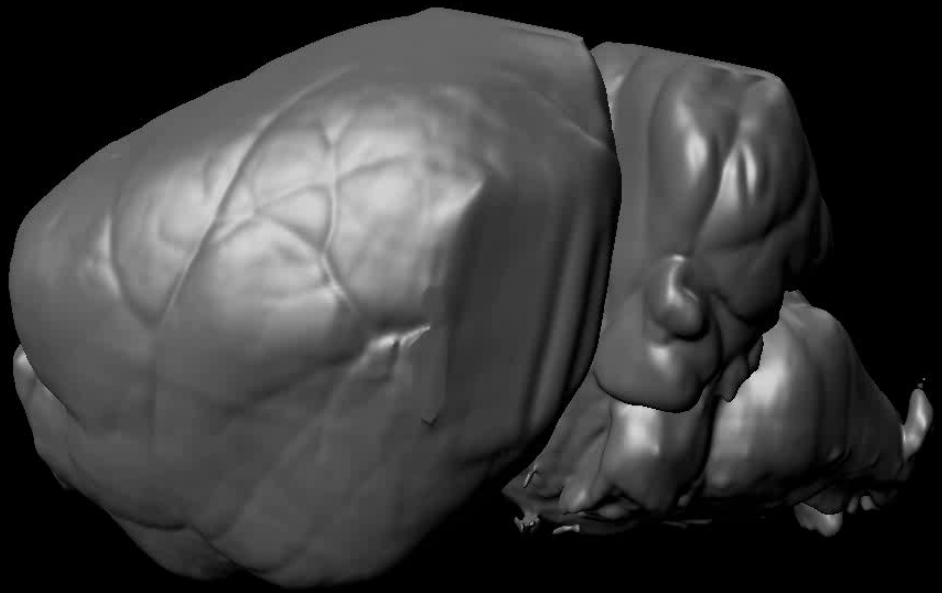
Central GLP-1 receptors mediate the weight lowering effects of liraglutide in mice



* $p<0.05$. GLP-1R, glucagon-like peptide-1 receptor

Sisley *et al. J Clin Invest* 2014;124:2456–63

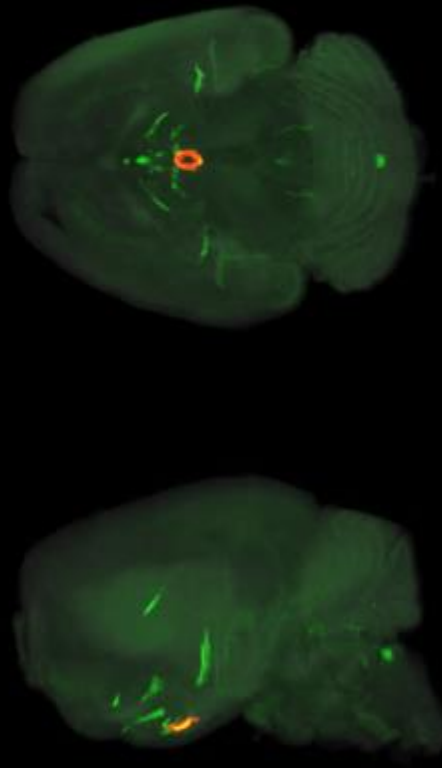
Liraglutide^{750} was detectable in the mouse brain following peripheral administration



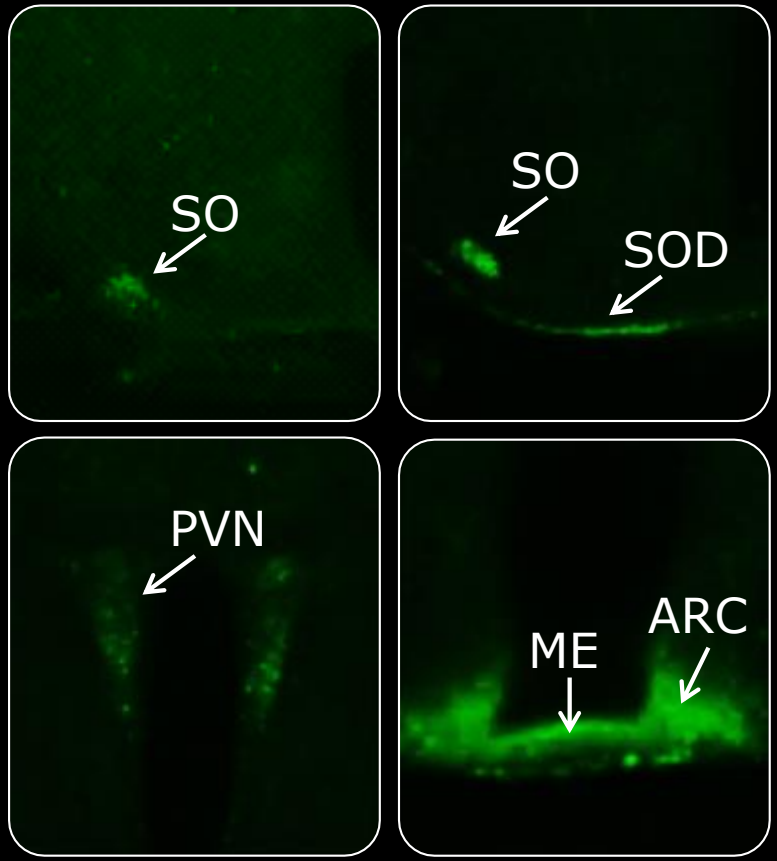
Peripheral (sc) injection of 120 nmol/kg ^{fluoro}liraglutide in mice for 4 days
Liraglutide^{750}

Secher *et al. J Clin Invest* 2014;124:4473–88

Liraglutide^{750} was detected in multiple regions of the mouse brain



Liraglutide^{750}



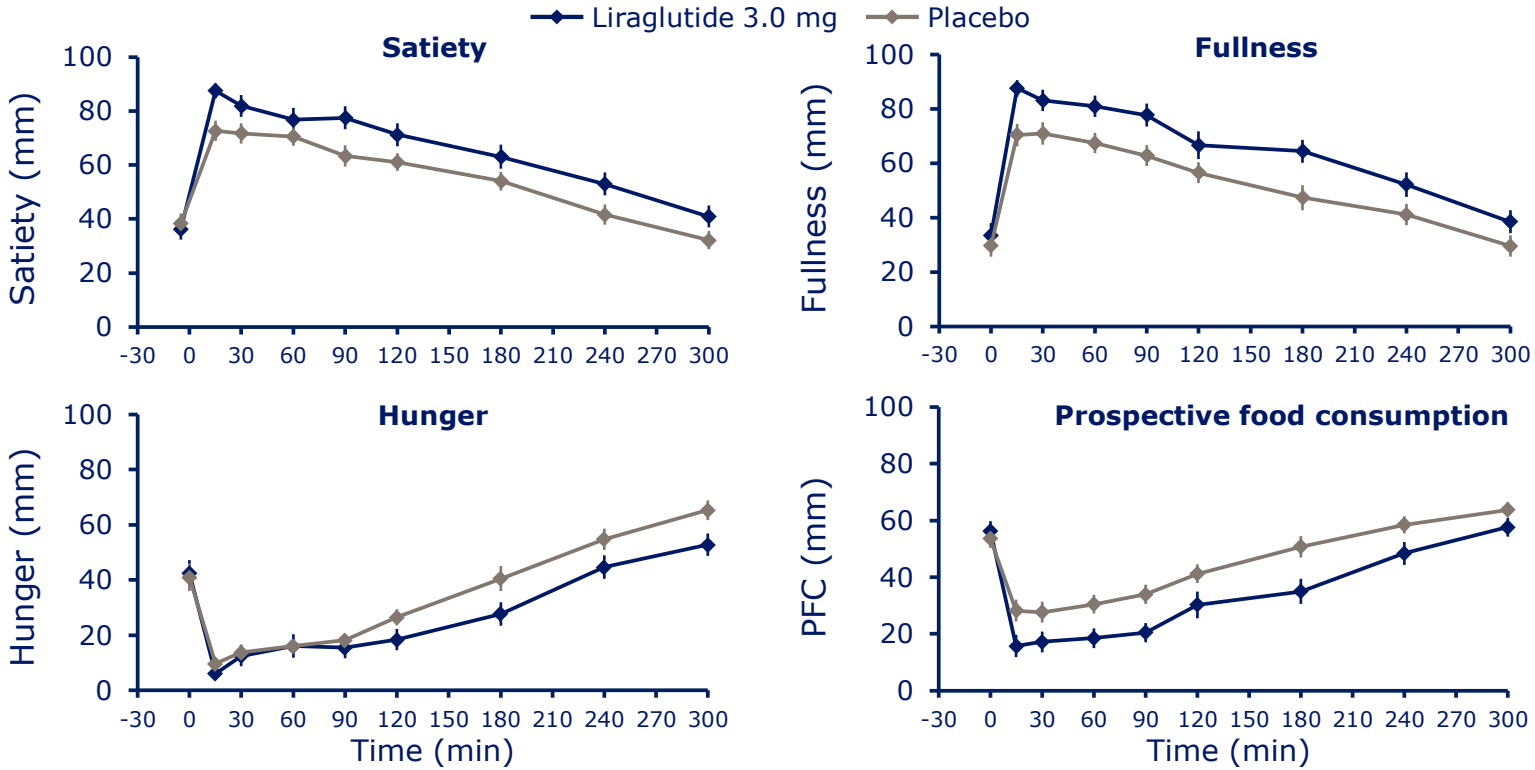
Liraglutide^{750}
6 hours

Secher *et al. J Clin Invest* 2014;124:4473–88

SO, supraoptic nucleus; SOD, supraoptic decussation

Liraglutide 3.0 mg influences all dimensions of appetite

Individuals with obesity and without diabetes: After 5 weeks of treatment

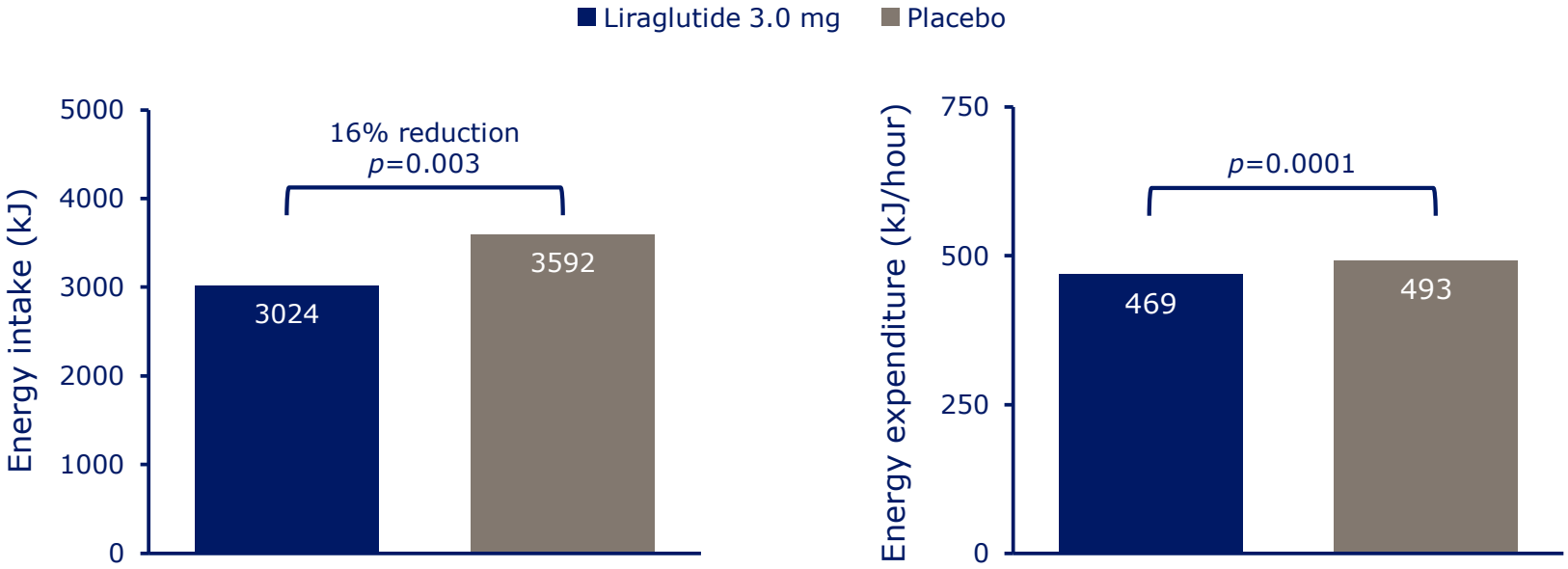


Appetite ratings were assessed by visual analog scale. Data are presented as mean ± standard error. PFC, prospective food consumption

Adapted from: van Can *et al. Int J Obes* 2014;38:784–93

Liraglutide 3.0 mg reduces energy intake but does not increase energy expenditure

Individuals with obesity and without diabetes: After 5 weeks of treatment

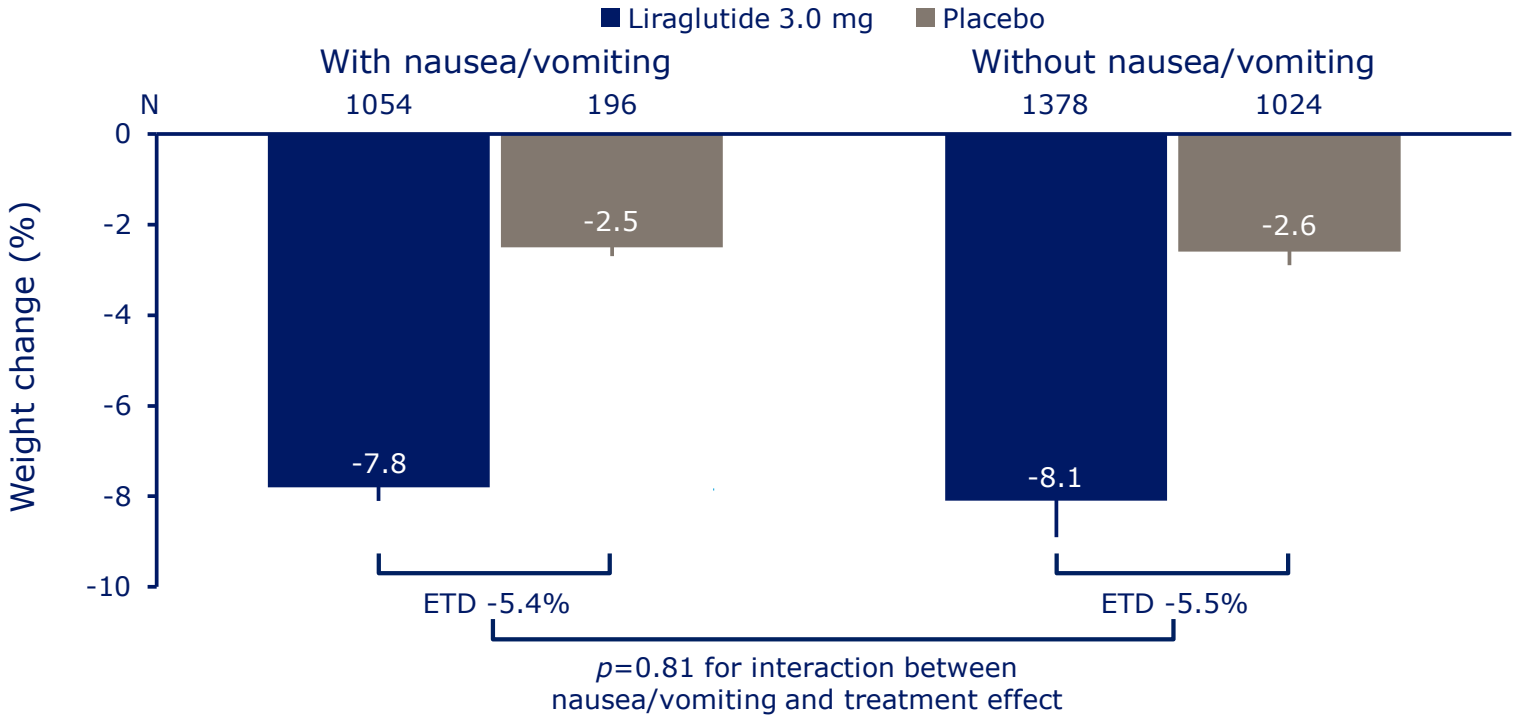


Data are estimated means. In the *post hoc* analysis for total energy expenditure, body weight after 5 weeks of treatment was added to the original linear mixed-effect model

Adapted from: van Can *et al. Int J Obes* 2014;38:784–93

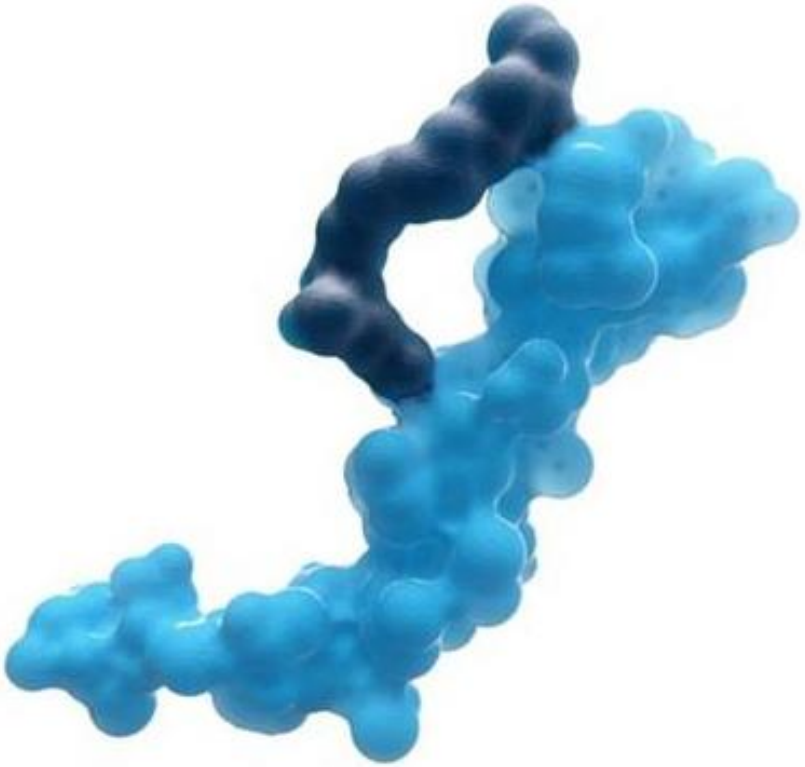
Weight loss with liraglutide 3.0 mg is not mediated by with nausea/vomiting

SCALE Obesity and Prediabetes: 56 weeks



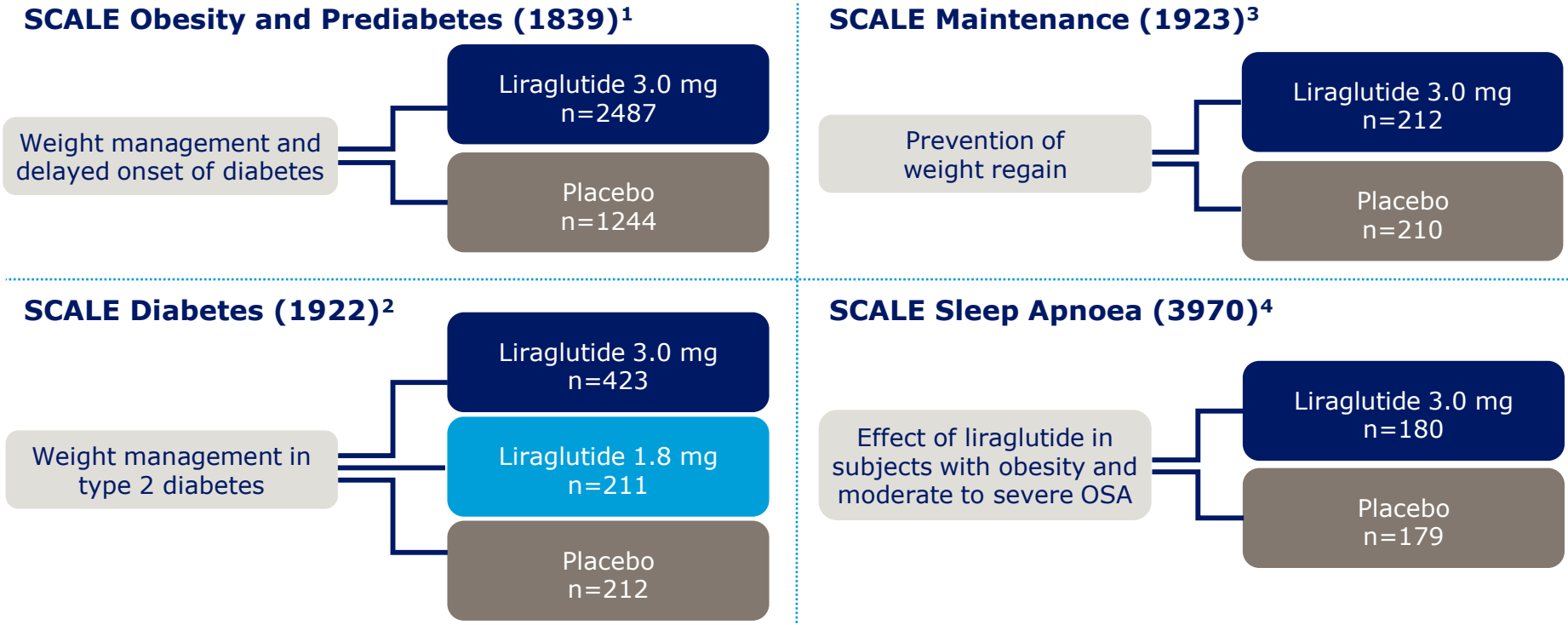
SCALE Obesity and Prediabetes. Least square means (± standard error); LOCF at end-of-treatment (56 weeks); ETD, estimated treatment difference; LOCF, last observation carried forward; N, number of subjects contributing to analysis

Lean *et al*. AACE 2015; Poster 611.



Liraglutide 3.0 mg in weight management

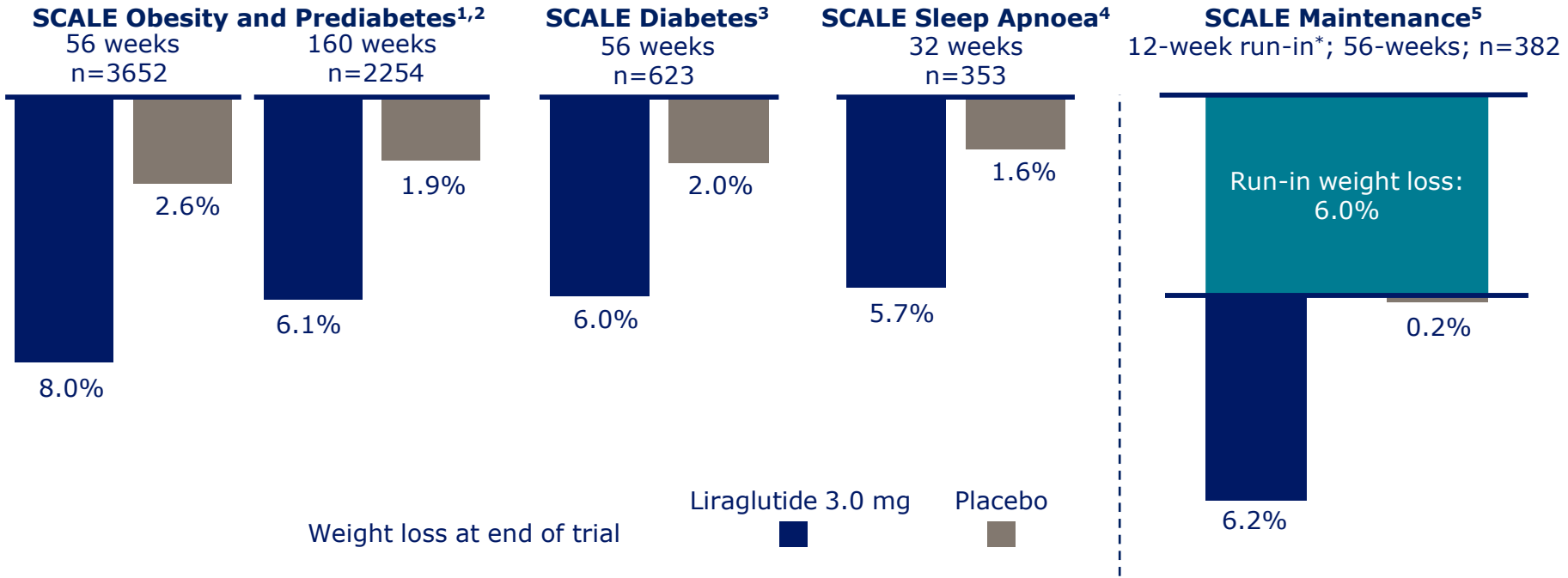
SCALE Phase 3a clinical trial programme



*SCALE, Sleep apnoea 3970 trial BMI ≥30 kg/m^2 plus co-morbidities;
BMI, body mass index; OSA, obstructive sleep apnoea; SCALE, Satiety and Clinical Adiposity – Liraglutide Evidence in individuals with and without diabetes

1. Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22; 2. Davies *et al. JAMA* 2015;314:687–99; 3. Wadden *et al. Int J Obes (Lond)* 2013;37:1443–51;
4. Blackman *et al. Int J Obes (Lond).* 2016;40:1310-9

Weight loss across SCALE trials



Data are observed means; last observation carried forward at end of trial; N, number of individuals contributing to the analysis
*Low calorie diet (total energy intake 1200–1400 kcal/day)

1. Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22; 2. le Roux CW *et al. Lancet.* 2017;389:1399–1409; 3. Davies *et al*. *JAMA* 2015;314:687–99;
4. Blackman *et al. Int J Obes (Lond)* 2016;40:1310–19; 5. Wadden *et al. Int J Obes (Lond)* 2013;37:1443–51

SCALE Efficacy Summary

Key efficacy outcomes with liraglutide 3.0 mg

SCALE Obesity and Prediabetes[1,2]

-8.0%

change in body weight after 1 year

80%

reduction in the risk of T2D over 3 years

SCALE Diabetes[3]

-6.0%

change in body weight after 56 weeks

-1.3%

change in HbA_{1c} from baseline

SCALE Maintenance[4]

81%

maintained ≥5% weight loss after 1 year

6.2%

additional weight loss with liraglutide 3.0 mg*

SCALE Sleep Apnoea[5]

-12.2

events p/h vs. 6.1 with placebo

-5.7%

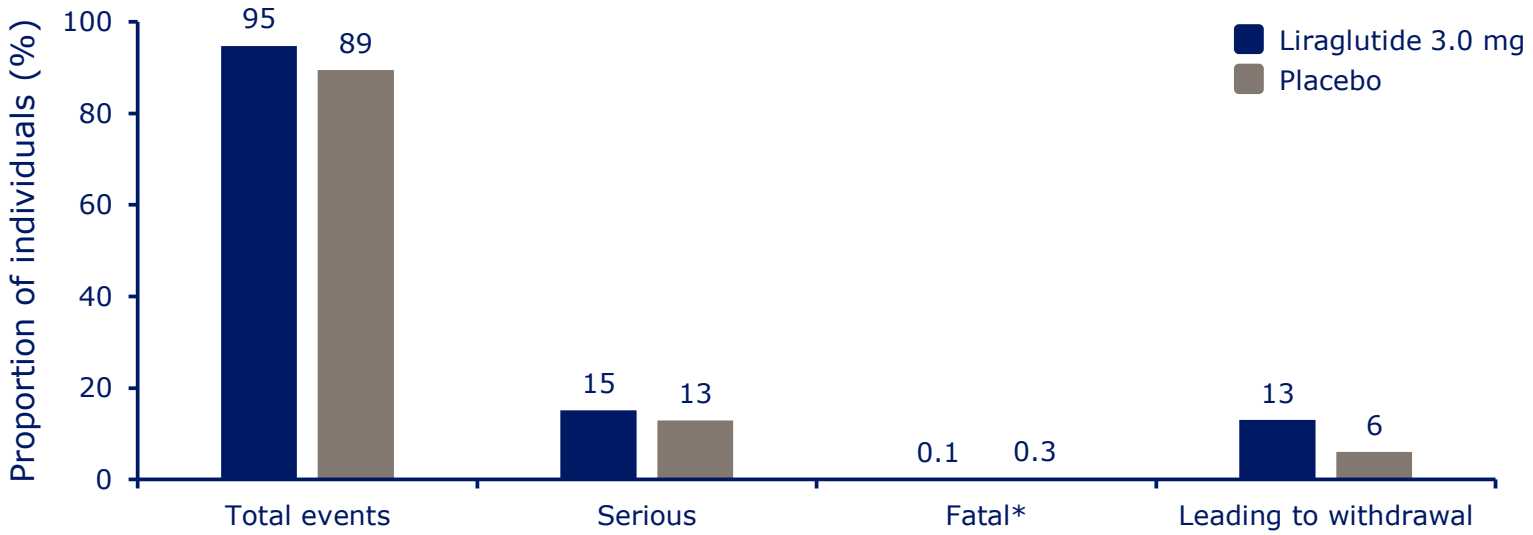
change in body weight after 32 weeks

*Following lifestyle intervention induced weight loss of ≥5% over a 12 week run in period

1. Pi-Sunyer *et al*. *N Engl J Med* 2015;373:11–22; 2. le Roux *et al*. *Lancet* 2017;389:1399–409; 3. Davies *et al*. *JAMA* 2015;314:687–99;
4. Wadden *et al*. *Int J Obes (Lond)* 2013;37:1443–51; 5. Blackman *et al. Int J Obes (Lond)* 2016;40:1310–19

Summary of treatment-emergent AEs

SCALE Obesity and Prediabetes: 0–162 weeks

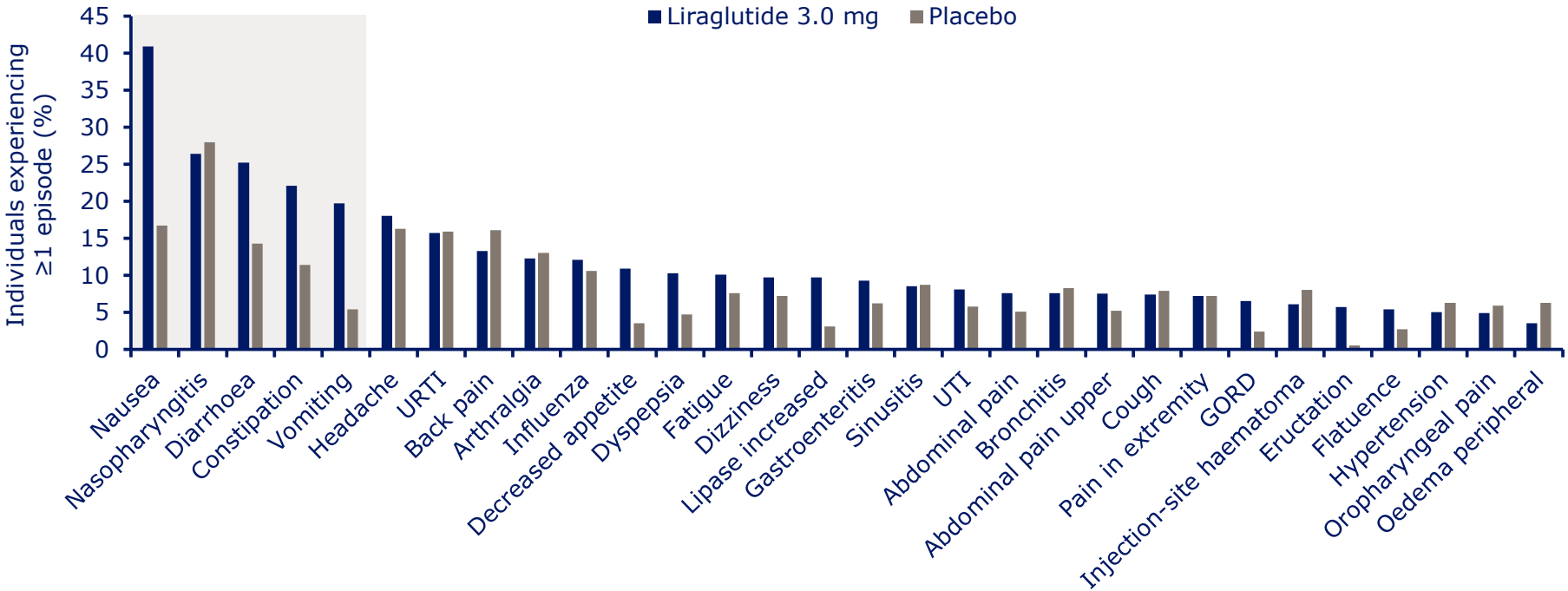


*n=2 liraglutide group (due to cardiac arrest and metastatic cholangiocarcinoma); n=2 placebo group(pulmonary failure and cancer, primary tumour unknown). Safety analysis set, 0–162 weeks. AE, adverse event.

le Roux et al. *Lancet* 2017;389:1399–409.

Adverse events in ≥5% of participants

SCALE Obesity and Prediabetes: 0–162 weeks

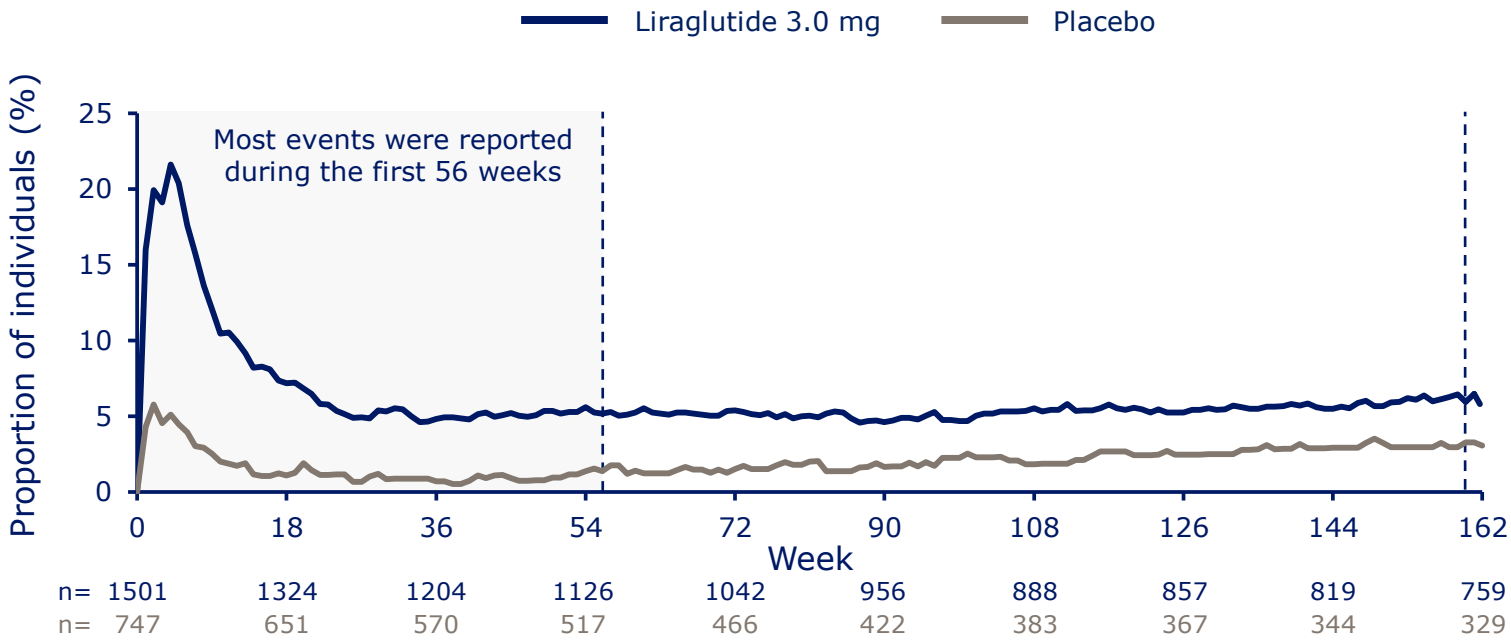


*GI, gastrointestinal; GORD, gastro-oesophageal reflux disease; SCALE, Satiety and Clinical Adiposity – Liraglutide Evidence in individuals with and without diabetes. URTI, upper respiratory tract infection; UTI, urinary tract infection. Safety analysis set. MedDRA search.

le Roux et al. *Lancet* 2017;389:1399–409.

Nausea over time

SCALE Obesity and Prediabetes: 0–162 weeks

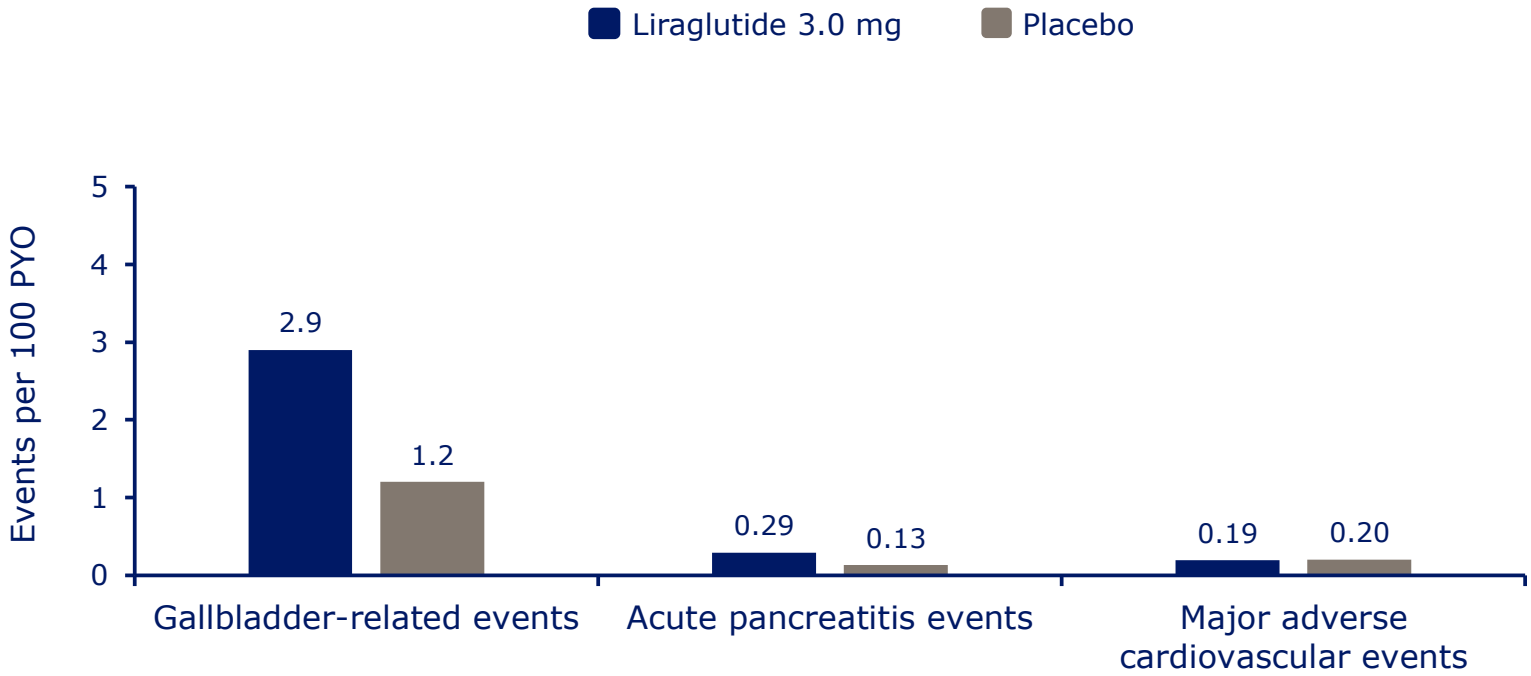


Observed mean data for the safety analysis set (liraglutide 3.0 mg n=1501; placebo n=747), 0–162 weeks.
Individuals were randomised 2:1 to liraglutide 3.0 mg and placebo

le Roux et al. *Lancet* 2017;389:1399–409.

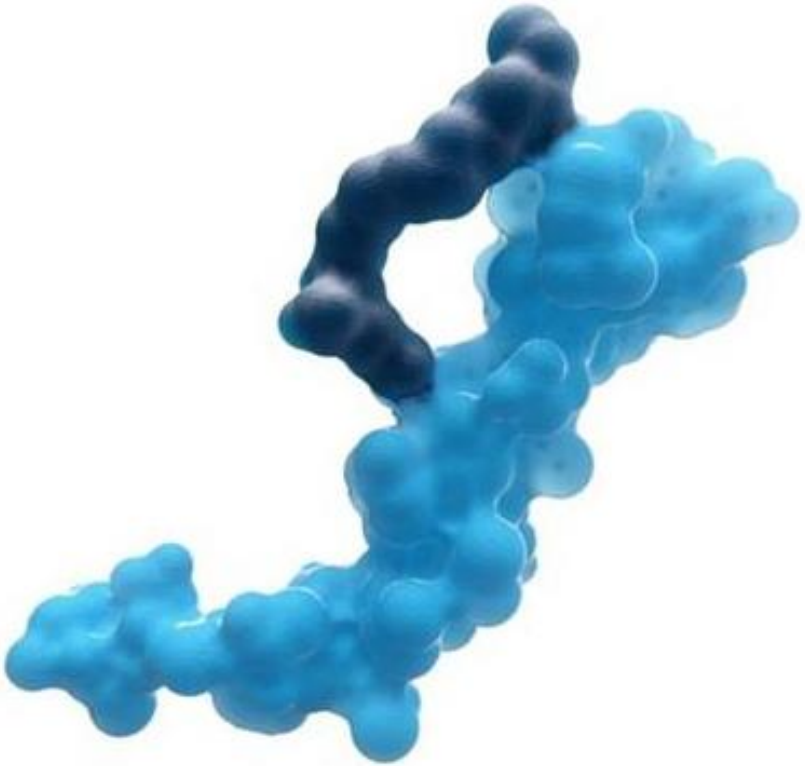
Adverse events of special interest

SCALE Obesity and Prediabetes



PYO, person–years of observation. Gallbladder-related and major adverse cardiovascular events are presented over 162 weeks. Acute pancreatitis events are presented over 172 weeks from the start of treatment until the final contact with the participant.

le Roux et al. *Lancet* 2017;389:1399–409.

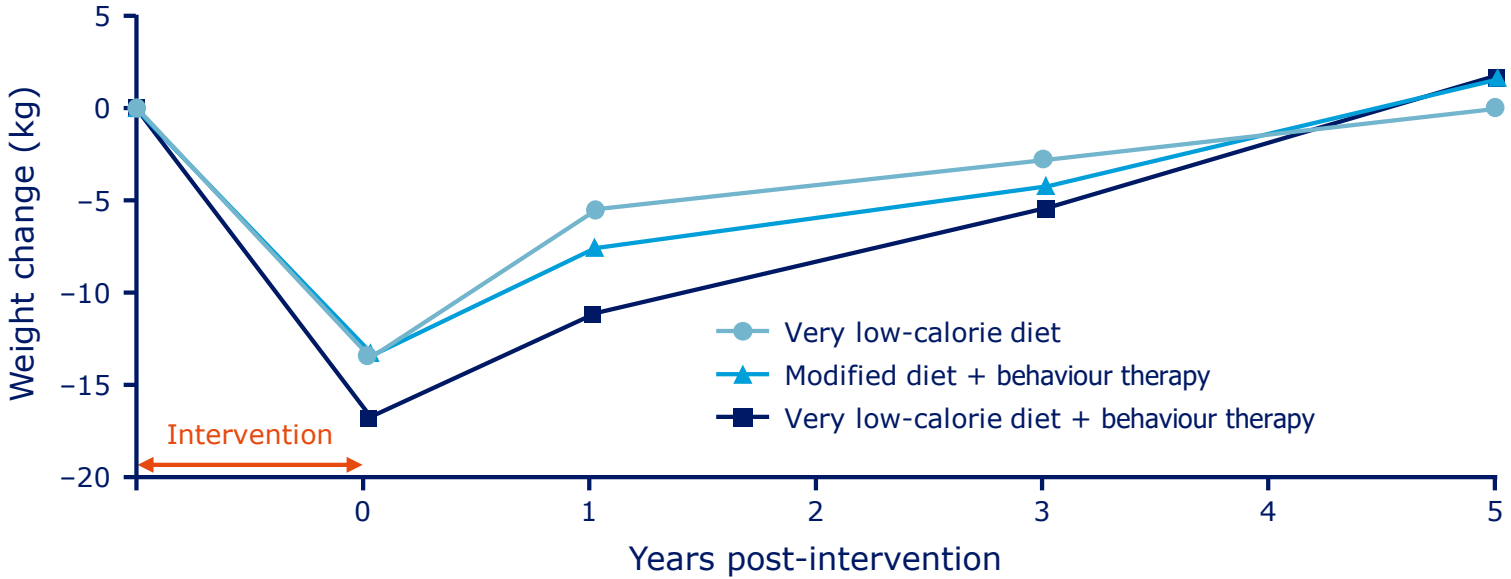


Clinical perspectives

Key aspects of weight management

- Achieving and maintaining a clinically relevant weight loss
- Improving cardiometabolic risk factors and health
- Reducing risk of diabetes
- Clinically relevant weight loss in patients with obesity and T2D

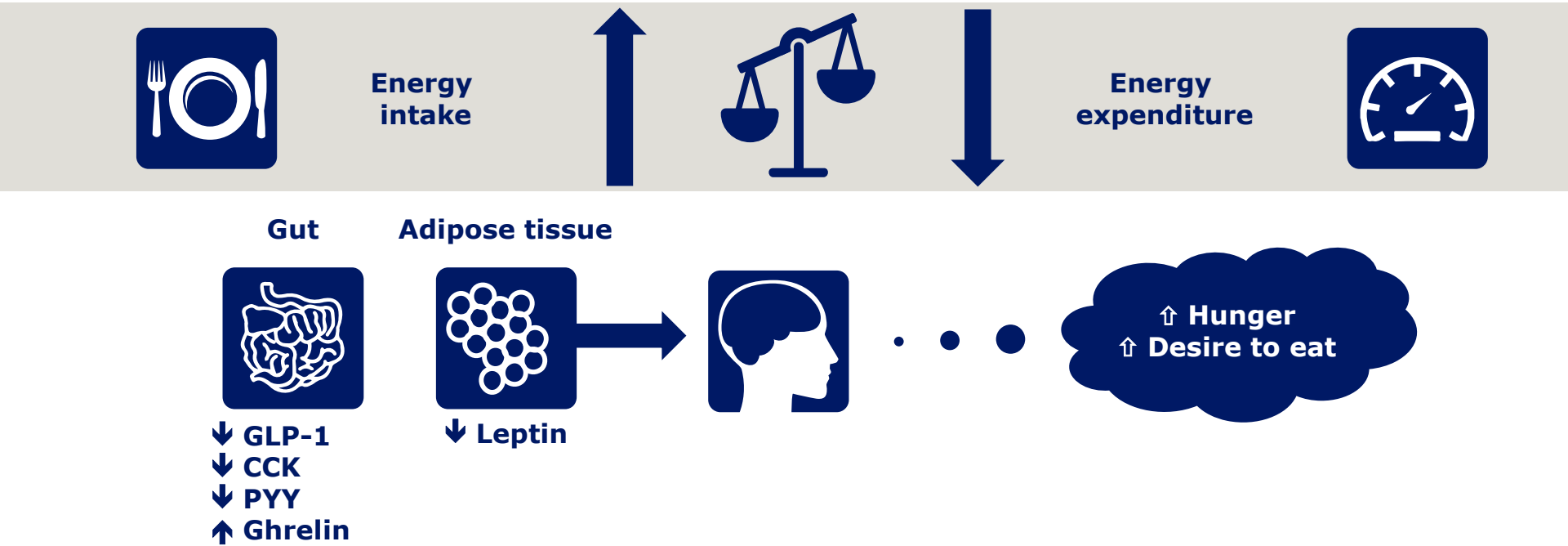
Weight management interventions are often followed by weight rebound



Data are from diet and behavioural interventions

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

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

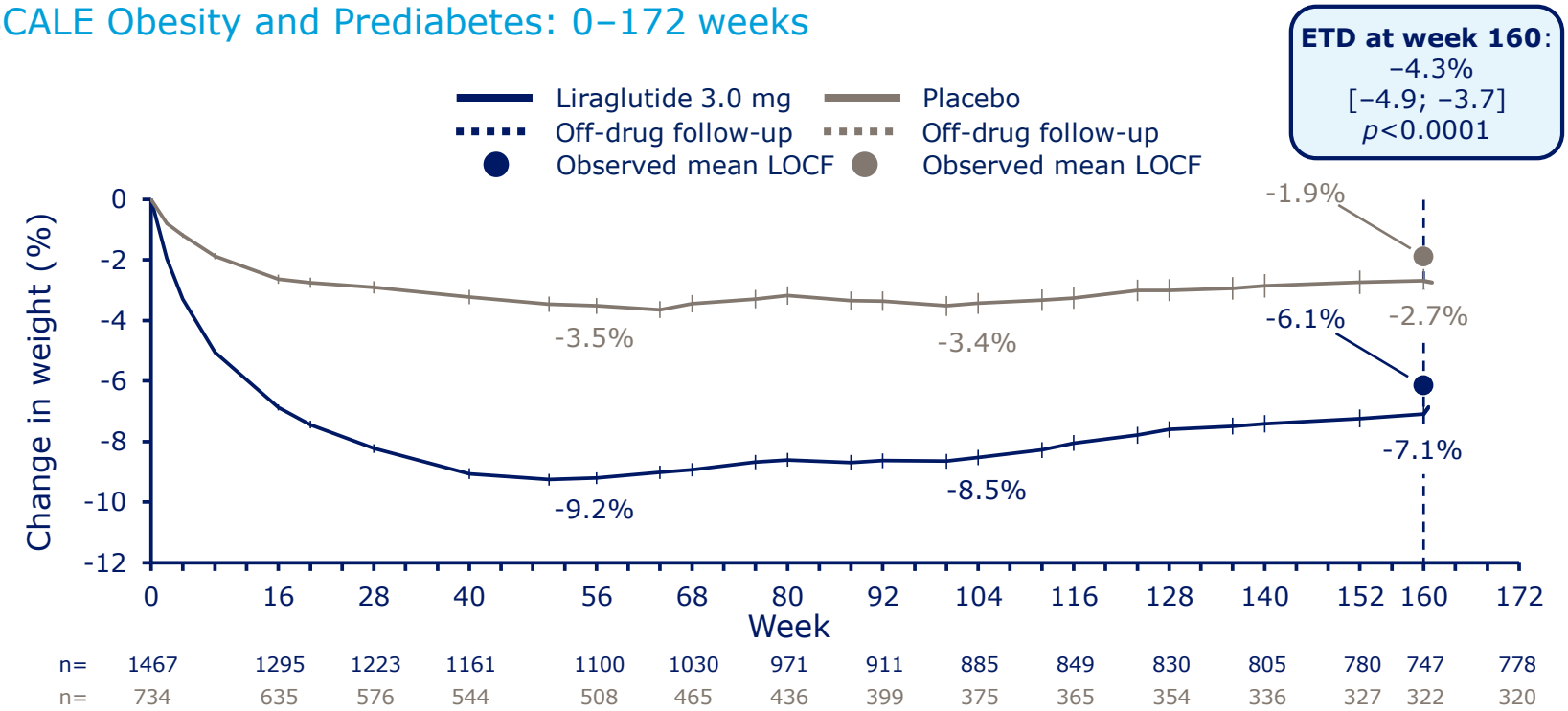


CCK, cholecystokinin; GLP-1, glucagon-like peptide-1; PYY, peptide YY

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

Change in body weight (%)

SCALE Obesity and Prediabetes: 0–172 weeks

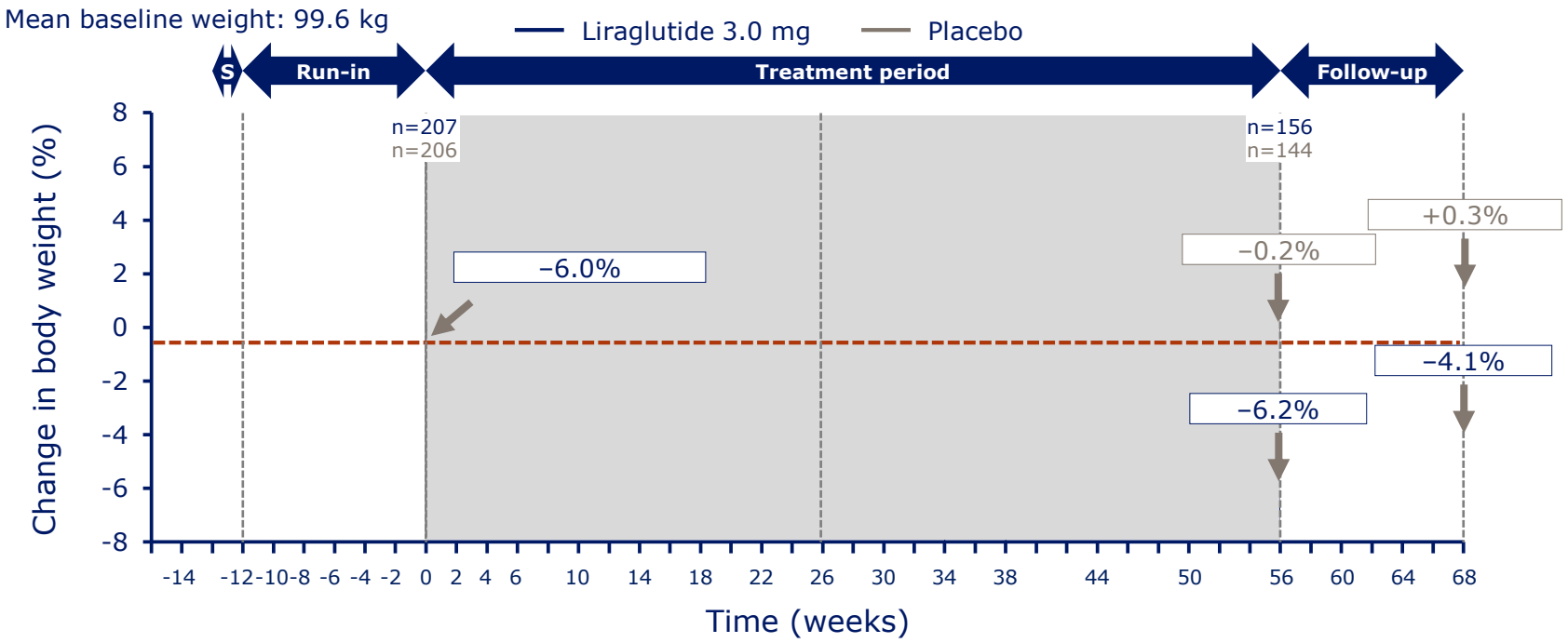


Full analysis set, fasting visit data only. Line graphs are observed means (±SE)
LOCF, last observation carried forward; SE, standard error

le Roux *et al*. *Lancet* 2017;389:1399–409

Change in body weight (%)

SCALE Maintenance



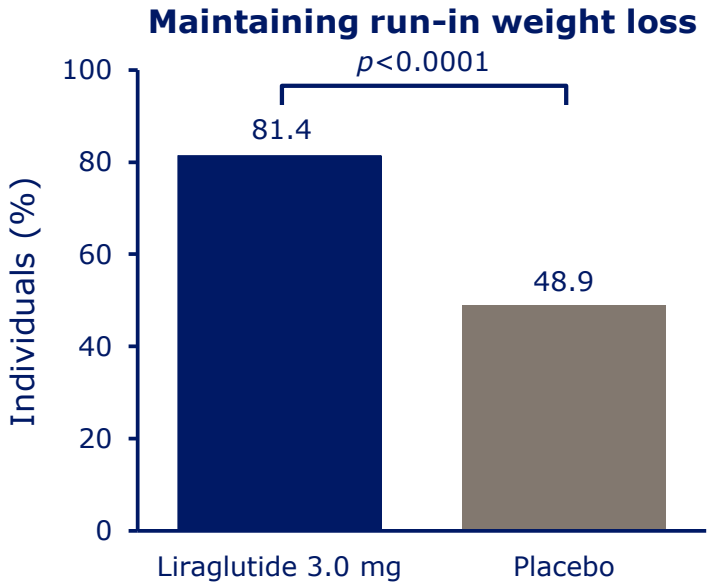
Mean (±SD); Full analysis set. S, screening period; SD, standard deviation

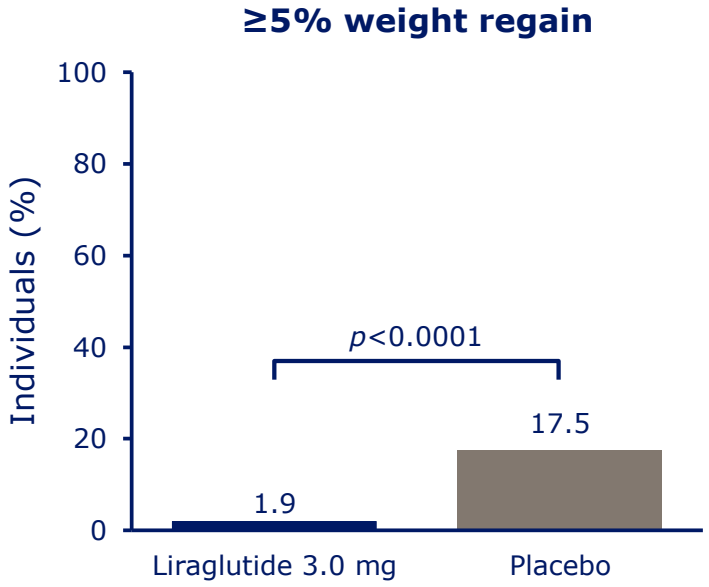
Wadden *et al. Int J Obes (Lond)* 2013;37:1443–51

Individuals maintaining or regaining weight loss

SCALE Maintenance: At week 56

Mean baseline weight: 99.6 kg





Full analysis set; LOCF at week 56. LOCF, last observation carried forward

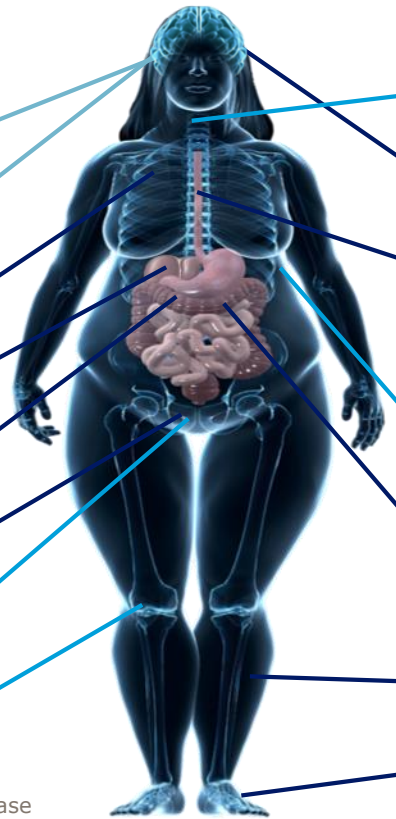
Wadden *et al. Int J Obes (Lond)* 2013;37:1443–51

Key aspects of weight management

- Achieving and maintaining a clinically relevant weight loss
- Improving cardiometabolic risk factors and health
- Reducing risk of diabetes
- Clinically relevant weight loss in patients with obesity and T2D

Obesity is associated with multiple comorbidities and complications

Metabolic, mechanical and mental



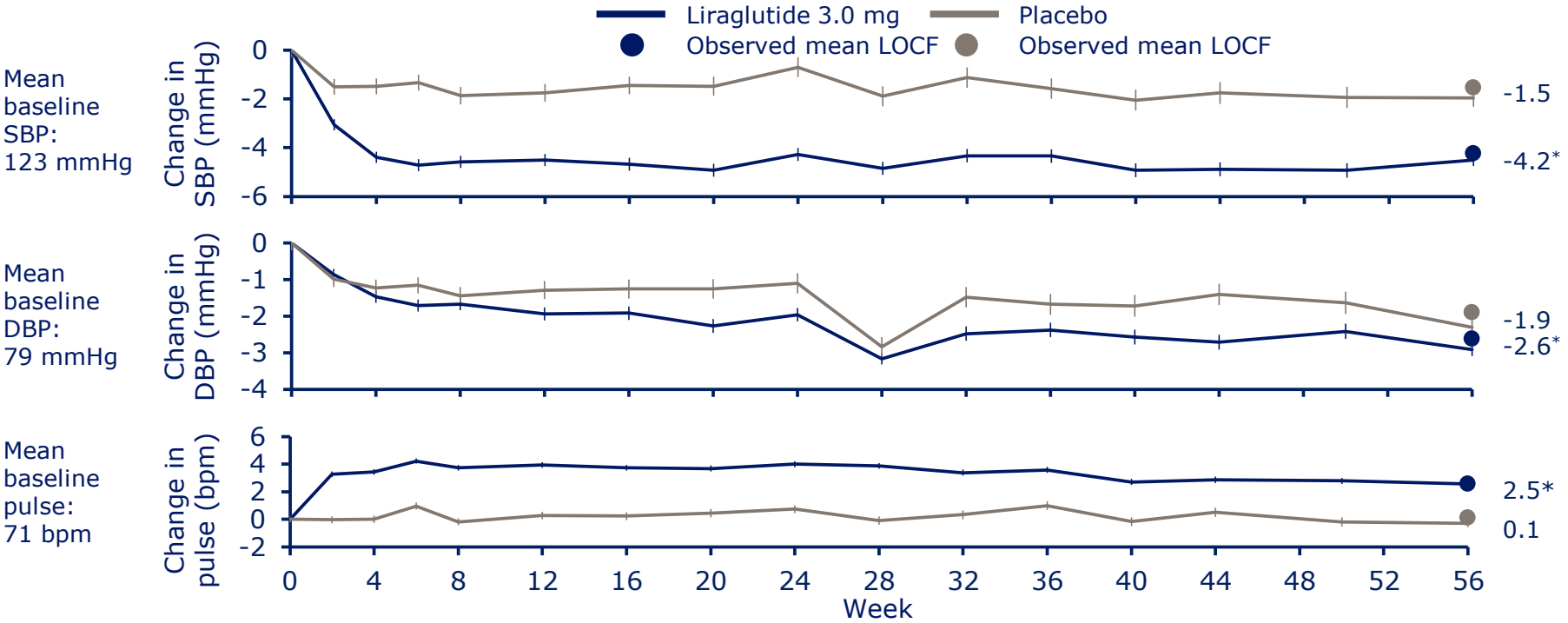
- Metabolic
- Mechanical
- Mental
- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Infertility
- Incontinence
- Arthrosis
- Cancers*
- Physical functioning
- Sleep apnoea
- CVD and risk factors
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - Congestive heart failure
  - 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

Changes in blood pressure and pulse

SCALE Obesity and Prediabetes: 0–56 weeks

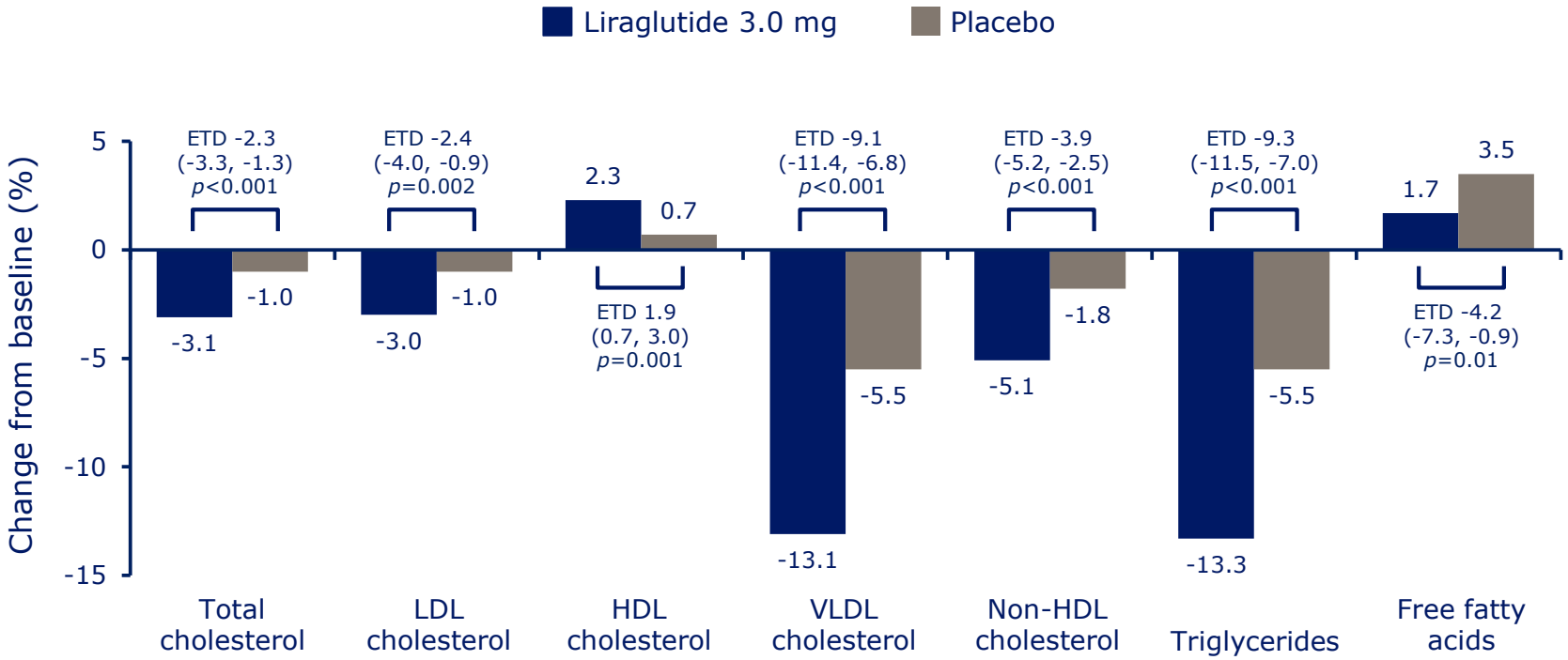


FAS, LOCF (blood pressure); SAS, LOCF (pulse). Data are observed means (±SE) of all participants attending each visit. Statistical analyses are ANCOVA. *$p<0.001$.
ANCOVA, analysis of covariance; bpm, beats per minute; DBP, diastolic blood pressure; FAS, full analysis set; LOCF, last observation carried forward; SAS, safety analysis set; SBP, systolic blood pressure; SE, standard error

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

Change in fasting lipids

SCALE Obesity and Prediabetes: 0–56 weeks

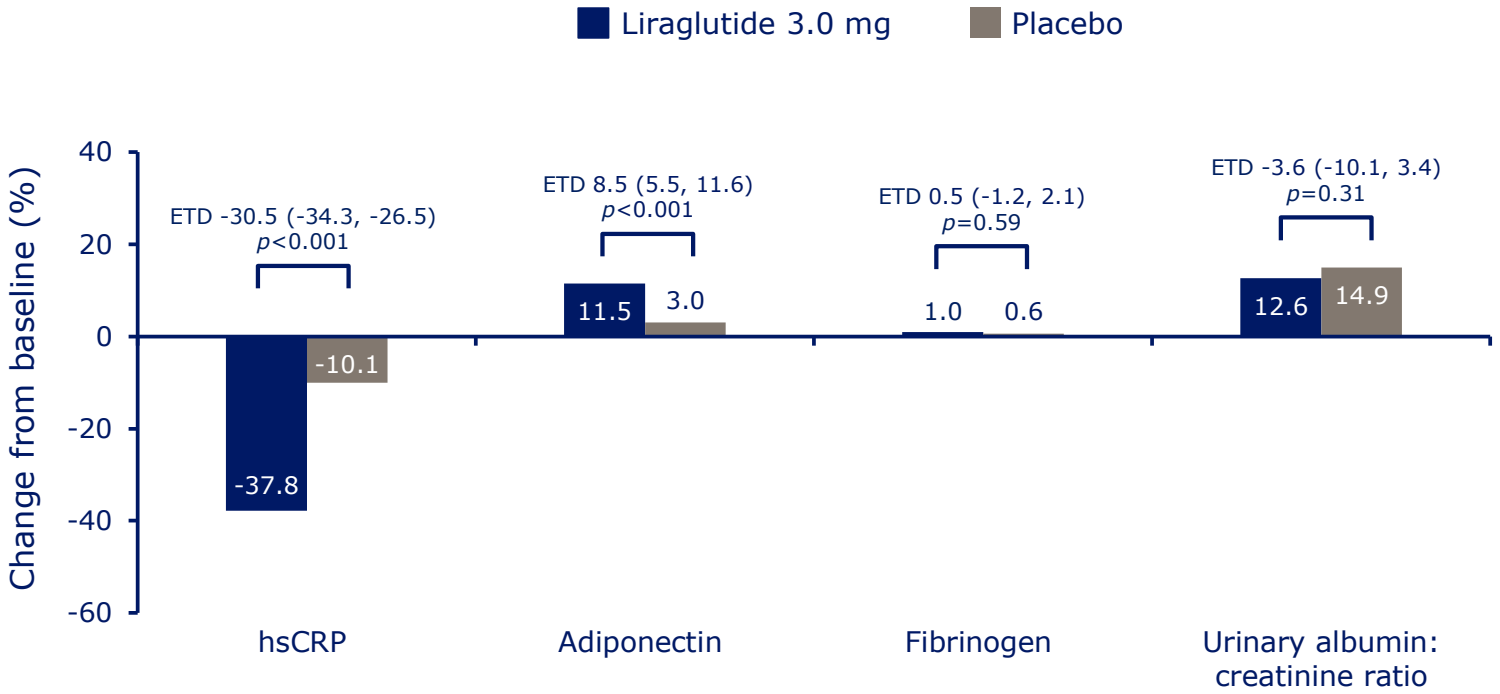


FAS, LOCF. Data are based on observed geometric means. Statistical analysis is ANCOVA. ETD, estimated treatment difference (95% CI); FAS, full analysis set; LOCF, last observation carried forward

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

Change in cardiovascular biomarkers

SCALE Obesity and Prediabetes: 0–56 weeks

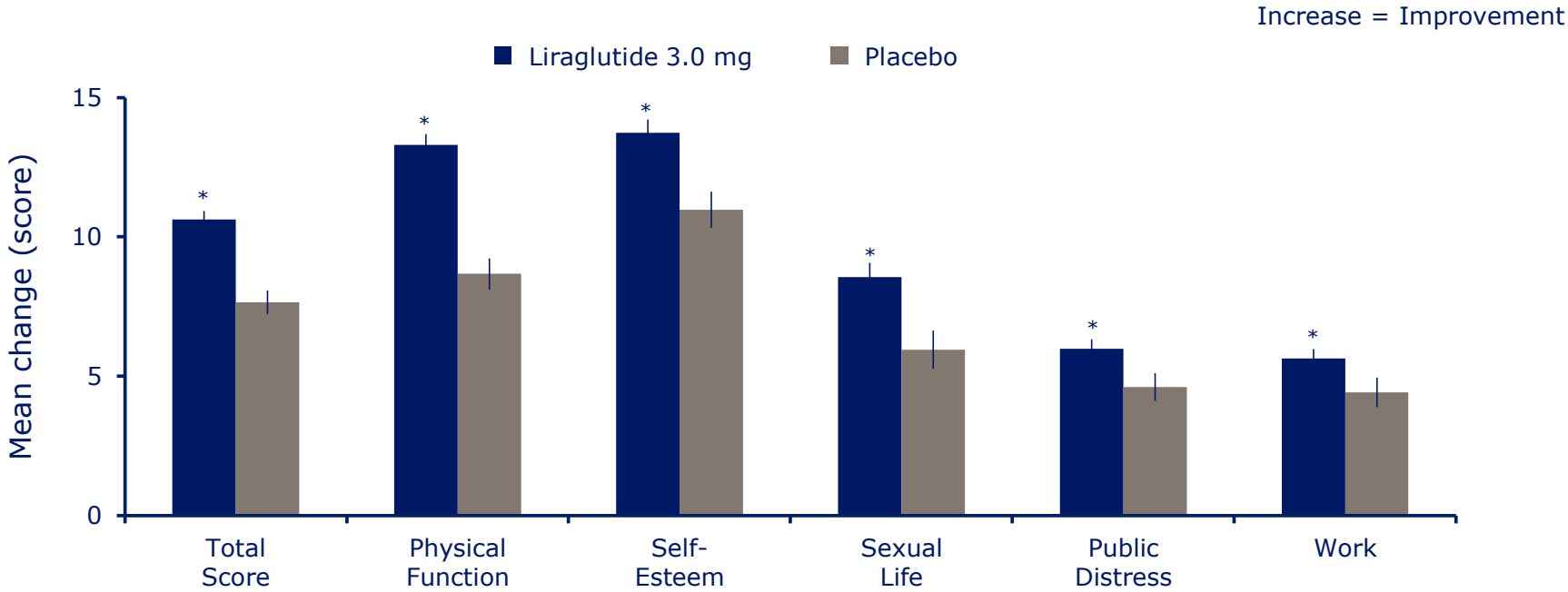


FAS, LOCF. Data are based on observed geometric means. Statistical analysis is ANCOVA. Data for PAI-1 not available. Data are shown as % change from baseline. Units of measure were hsCRP (mg/L); Adiponectin (mg/L); Fibrinogen (g/L); Urinary albumin: creatinine ratio (mg/mol). FAS, full analysis set; ETD, estimated treatment difference (95% CI); LOCF, last observation carried forward

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

Summary of IWQOL-Lite

SCALE Obesity and Prediabetes: 0–56 weeks



FAS LOCF. Bar graph is observed mean change from baseline. Statistical analysis is ANCOVA. *$p<0.01$
FAS, full analysis set; IWQOL-Lite, Impact of weight on quality of life-lite questionnaire; LOCF, last observation carried forward

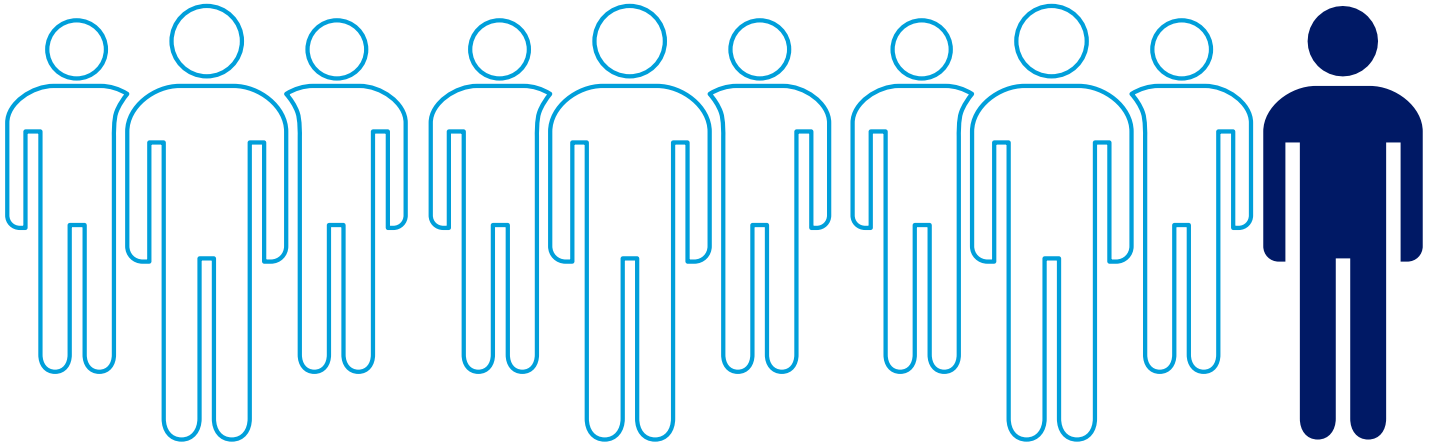
Pi-Sunyer *et al. N Engl J Med* 2015;373:11–22

Key aspects of weight management

- Achieving and maintaining a clinically relevant weight loss
- Improving cardiometabolic risk factors and health
- Reducing risk of diabetes
- Clinically relevant weight loss in patients with obesity and T2D

Awareness of prediabetes remains low

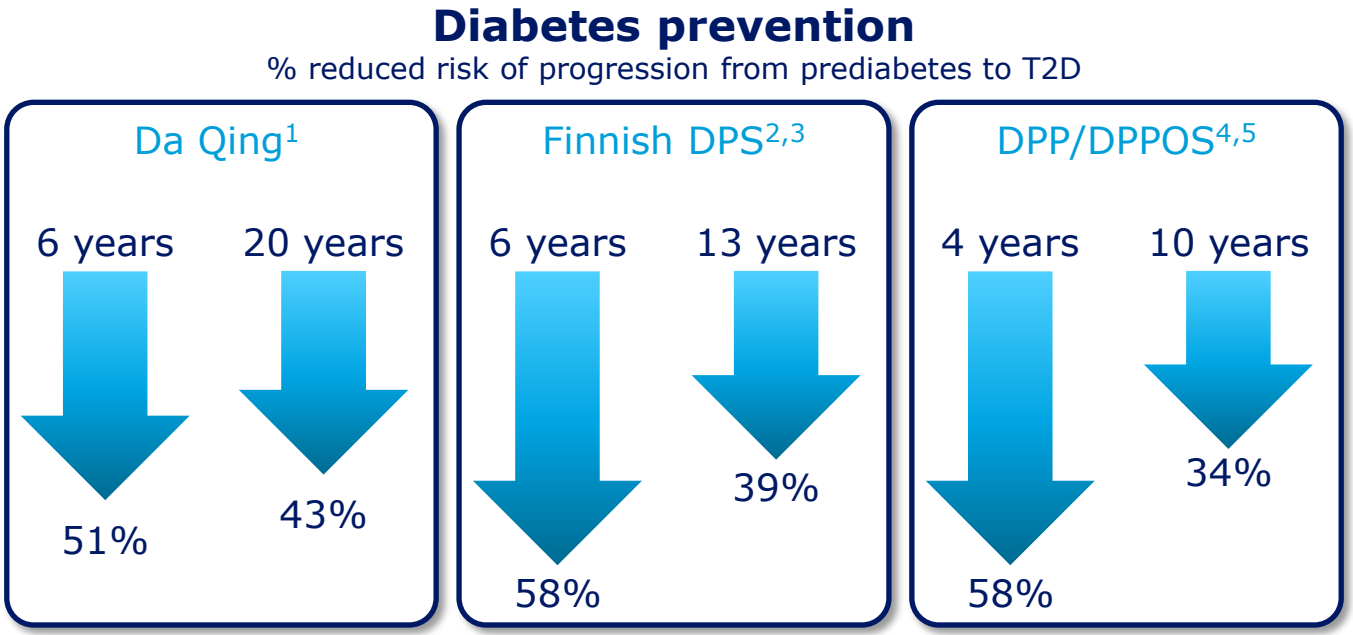
9 out of 10 individuals
with prediabetes do not know that they have it



Data presented is US population
Prediabetes defined as FPG 5.6–6.9 mmol/L [100–125 mg/dL] or HbA_{1c} 5.7–6.4%
CDC, Center for Disease Control; FPG, fasting plasma glucose; NHANES, National Health and Nutrition Examination Survey

Li et al. *MMWR* 2013;62:209-212; Pal et al. *US Pharm*. 2018;43(10):48.

Benefits of weight loss on diabetes risk

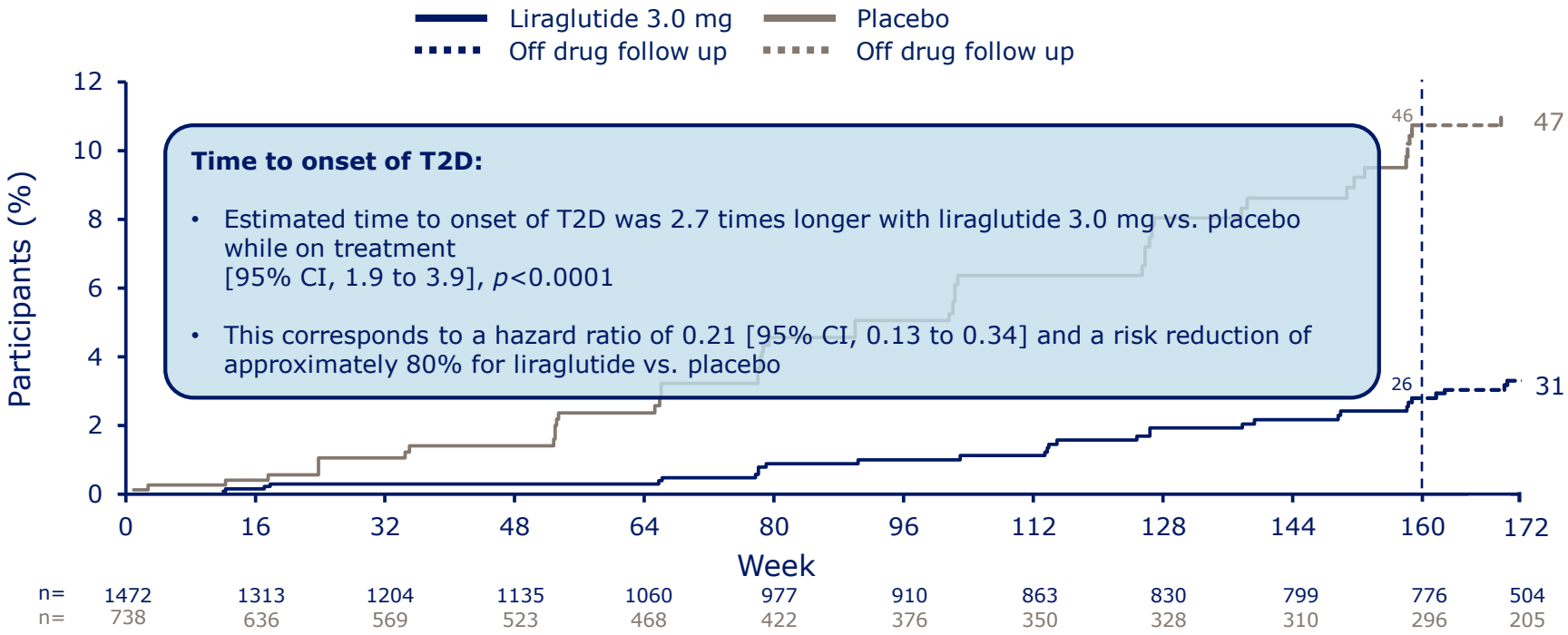


BP, blood pressure; DiRECT, Diabetes Remission Clinical Trial; DPP, Diabetes Prevention Programme; DPPOS, Diabetes Prevention Programme Outcomes Study; DPS, Diabetes Prevention Study; AHEAD, Action for Health Diabetes; ILI, intensive lifestyle intervention; T2D, type 2 diabetes

1. Li et al. Lancet 2008;371:1783–9; 2. Tuomilehto et al. N Engl J Med 2001;344:1343–50; 3. Lindström et al. Lancet 2006;368:1673–9; 4. Knowler et al. N Engl J Med 2002;346:393–403; 5. Knowler et al. Lancet 2009;374:1677–86

Participants diagnosed with T2D over time

SCALE Obesity and Prediabetes - Kaplan–Meier plot: 0–172 weeks

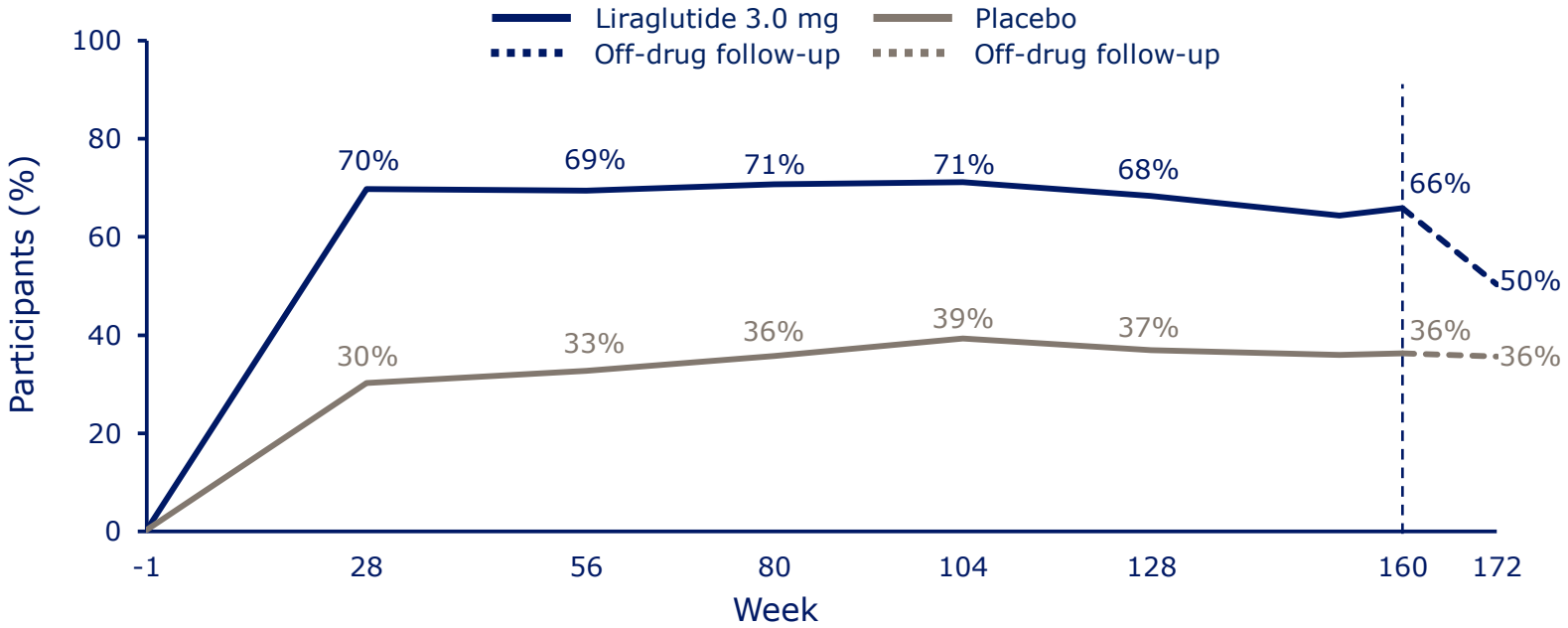


Full analysis set. Numbers in the figure correspond to the accumulated number of diagnosed participants
T2D, type 2 diabetes

le Roux *et al*. *Lancet* 2017;389:1399–409

Regression to normoglycaemia over time

SCALE Obesity and Prediabetes: 0–172 weeks



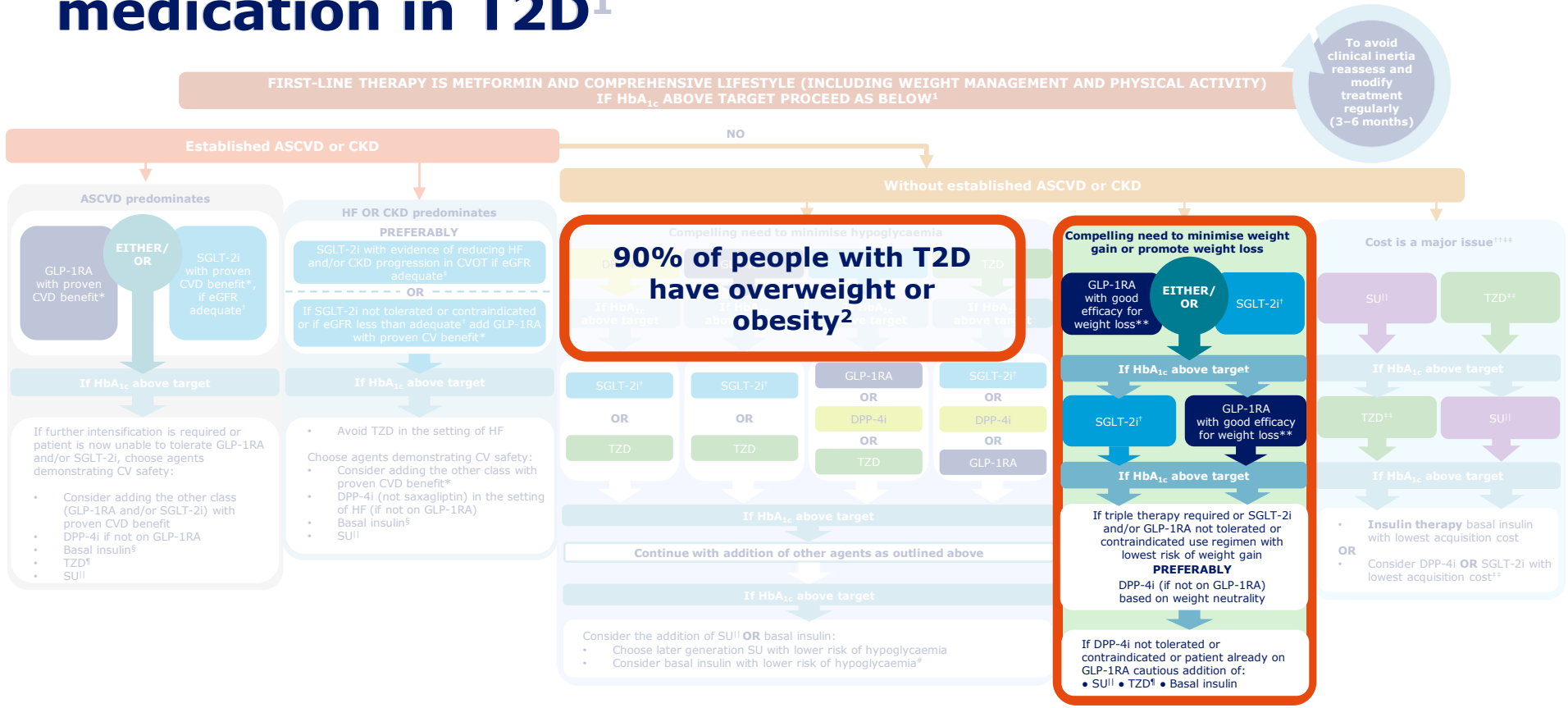
Full analysis set, last observation carried forward. Statistical analysis is logistic regression (OR with 95% CI). Normoglycaemia is defined as fasting plasma glucose <100 mg/dL (<5.6 mmol/L) and/or 2-hour post-challenge glucose <140 mg/dL (<7.8 mmol/L) and/or HbA_{1c} <5.7%. Data measured at OGTT visits.
CI, confidence interval; NNT, number needed to treat; OR, estimated odds ratio

le Roux *et al*. *Lancet* 2017;389:1399–409

Key aspects of weight management

- Achieving and maintaining a clinically relevant weight loss
- Improving cardiometabolic risk factors and health
- Reducing risk of diabetes
- Clinically relevant weight loss in patients with obesity and T2D

ADA/EASD 2018 consensus for glucose-lowering medication in T2D[1]

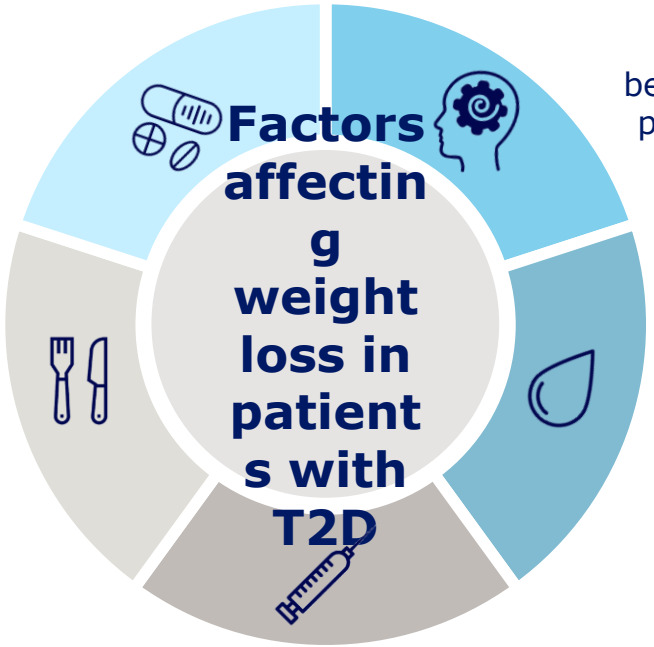


1. Davies et al. *Diabetologia* 2018;61(12):2461–98;
2. World Health Organization report on Obesity and Overweight. Available at: http://www.who.int/dietphysicalactivity/media/en/gsfs_obesity.pdf (Last accessed: Aug 2019)

Challenge of weight loss in patients with T2D

Many conventional glucose-lowering agents and even concomitant medications favour weight gain[4,5]

Metabolic, psychological, and behavioural factors affect ability of people with T2D to lose weight[1,2]



Compensatory eating for fear of hypoglycaemia[7]

Improved glycaemic control decreases glycosuria, which may impair weight loss[3]

Insulin inhibits lipolysis and promotes lipogenesis[6]

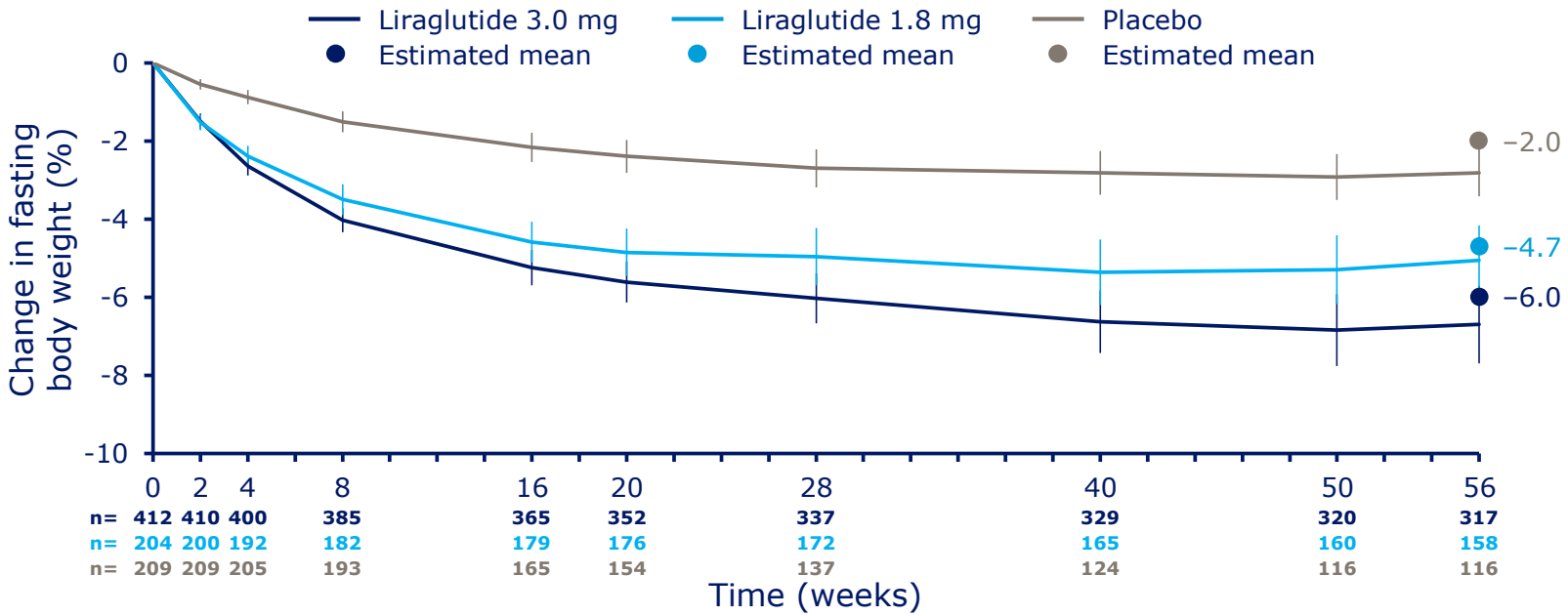
T2D, type 2 diabetes

1. Cabrera J et al. *Curr Med Res Opin* 2012;28:1027–37; 2. Scheen AJ et al. *Diabetes Metab* 2007;33:169–75; 3. Rosenbaum M et al. *J Clin Invest* 2008;118:2583–91; 4. UKPDS. *Lancet* 1998;352:837–53; 5. ACCORD. *Diabetes Care* 2013;36:2162–8; 6. Eriksson H et al. *Biochim Biophys Acta* 1995;1266:101–7; 7. Yki-Jarvinen H et al. *J Clin Endocrinol Metab* 1997;82:4037–43

Change in body weight (%)

SCALE Diabetes: 0-56 weeks

Mean baseline body weight: 105.9 kg

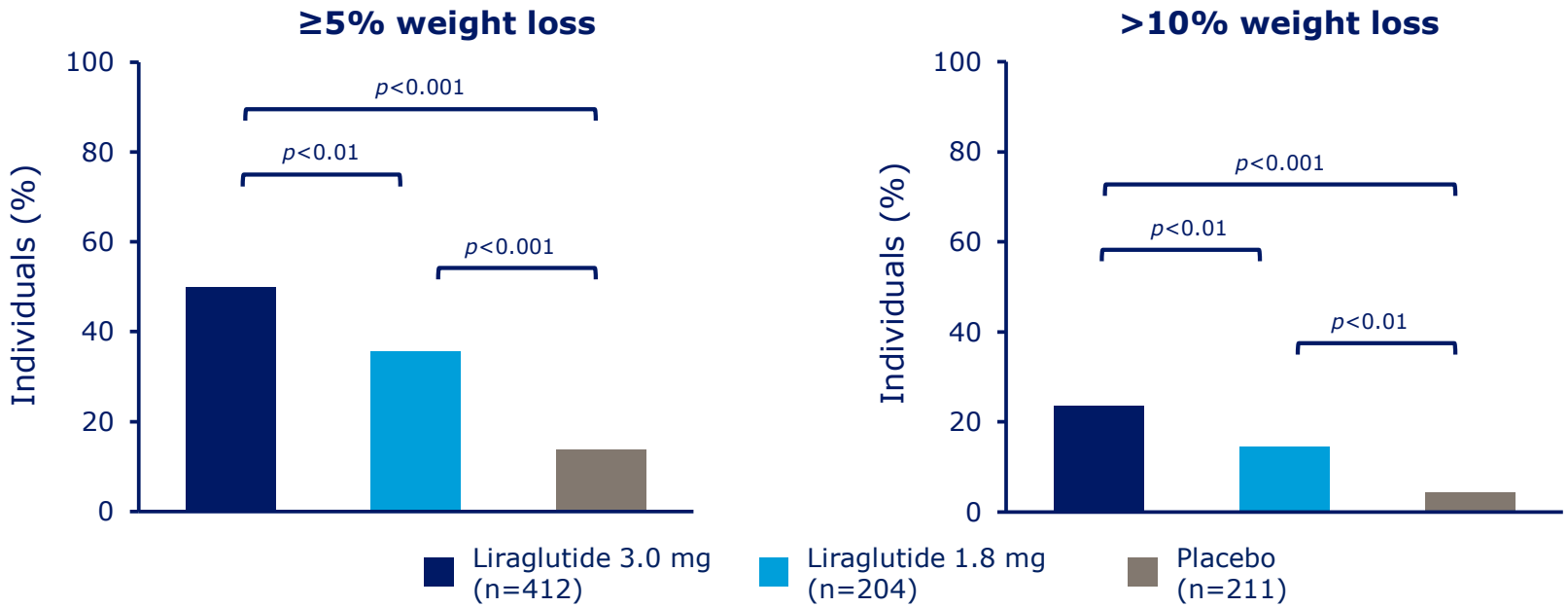


FAS. Line graphs are observed means (±95% Wald CI). Statistical analysis is ANCOVA. Estimated means are calculated with missing observations at week 56 imputed using a regression method. ANCOVA, analysis of covariance; CI, confidence interval; FAS, full analysis set

Davies *et al*. *JAMA* 2015;314:687–99

Categorical weight loss (%)

SCALE Diabetes: 0-56 weeks



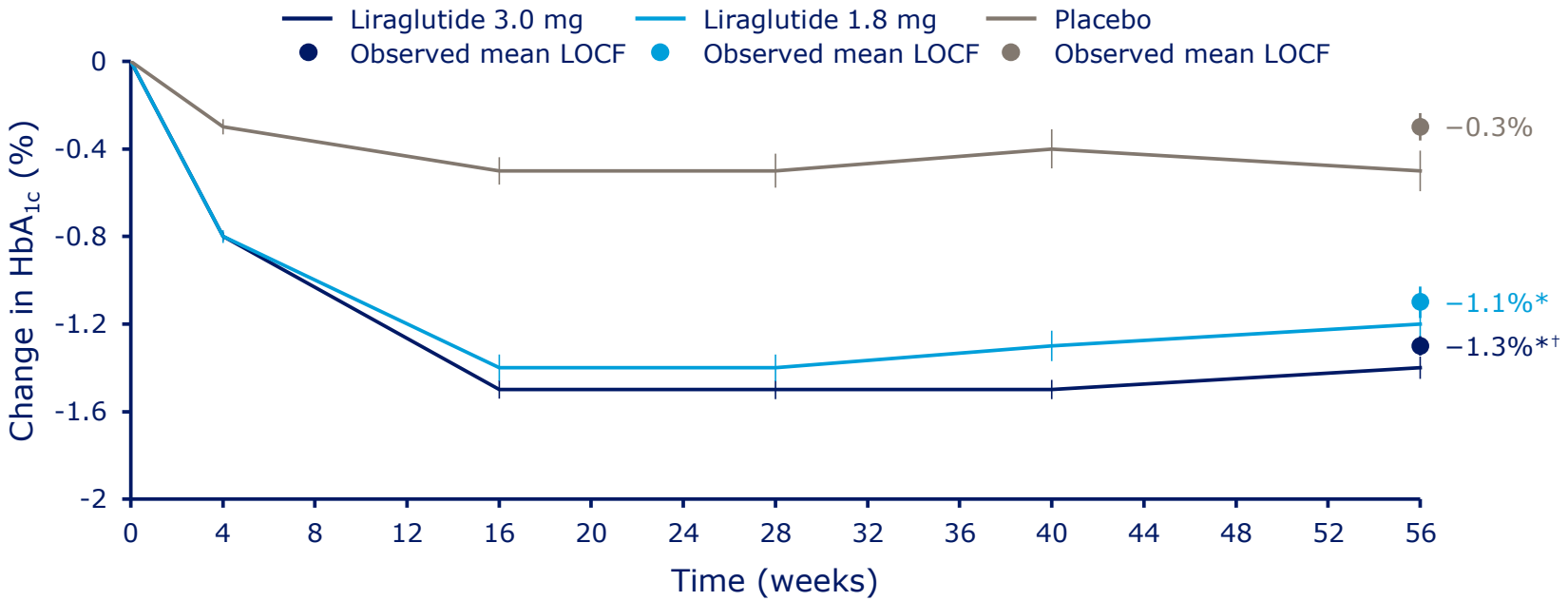
FAS, fasting visit data only, LOCF. Graphs are observed proportions LOCF. Statistical analysis is logistic regression
FAS, full analysis set; LOCF, last observation carried forward

Davies *et al*. *JAMA* 2015;314:687–99

Change in HbA_{1c} (%)

SCALE Diabetes: 0-56 weeks

Mean baseline HbA_{1c}: 8.0%

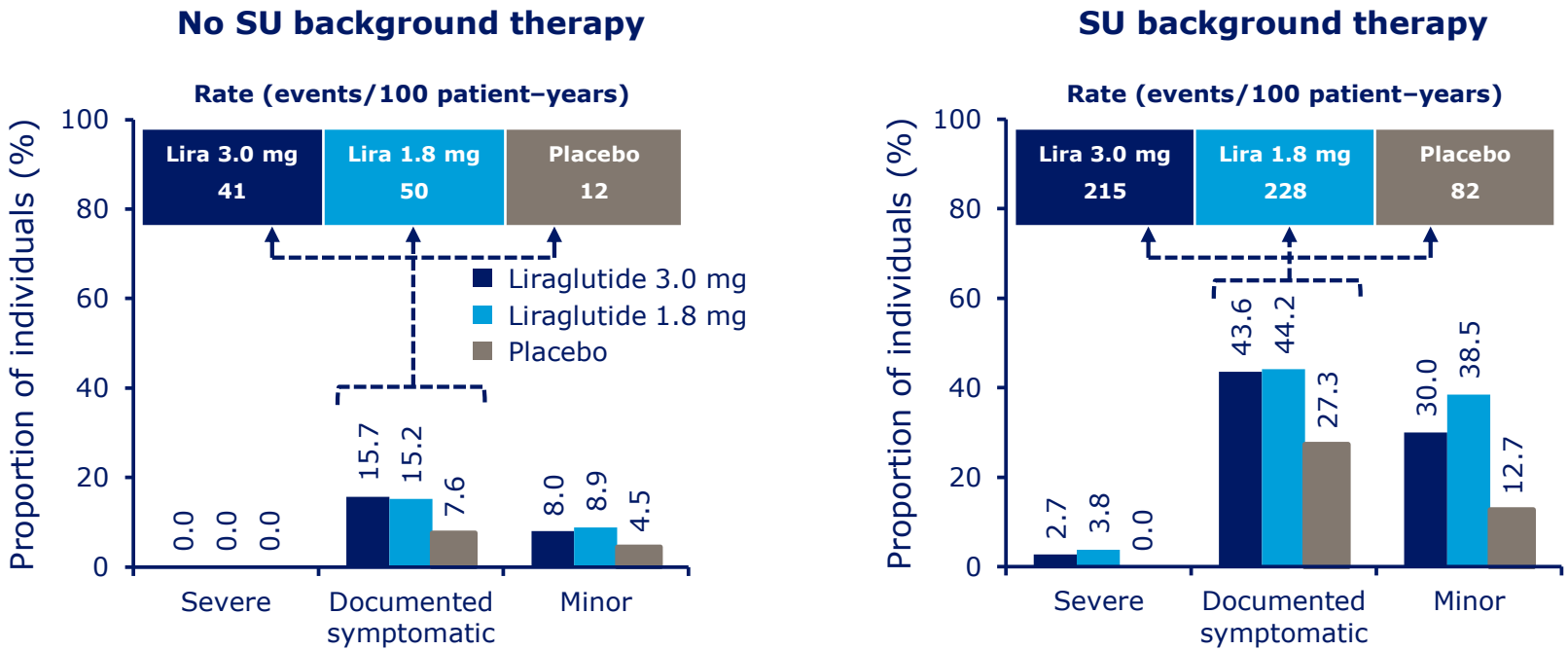


FAS LOCF. Line graphs are observed means (±SE). Circles are observed means LOCF.
FAS, full analysis set; LOCF, last observation carried forward; SE, standard error

Davies *et al. Diabetologia* 2014;57(Suppl. 1):Abstract 39-OR

Hypoglycaemic episodes by baseline SU status

SCALE Diabetes: 0-56 weeks



Safety analysis set. Rate is the event rate per 100 patient–years of exposure. Minor denotes minor hypoglycaemia where plasma glucose <3.1 mmol/L [56 mg/dL]. Documented symptomatic denotes plasma glucose ≤3.9 mmol/L [70 mg/dL] and symptoms typical of hypoglycaemia; hyperglycaemic episodes were defined according to ADA definitions (ADA. *Diabetes Care* 2010;33(Suppl.1):S62–69). ADA, American Diabetes Association; Lira, liraglutide; SU, sulphonylurea

Davies *et al*. *JAMA* 2015;314:687–99

Summary

- Central appetite regulation is complex and influenced by both homeostatic (metabolic) and hedonic (pleasure, emotional) factors
- GLP-1 increases satiety and reduces hunger by activating areas in the brain involved in appetite regulation
- Liraglutide 3.0 mg, a human GLP-1 analog, lowers body weight by lowering food intake
- Liraglutide 3.0 mg in combination with diet and exercise can help patients achieve a clinically relevant weight loss