

Title: Obesity in Primary Care

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Date: April 23rd

once weekly
mounjaro[™]
(tirzepatide) injection



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Dr Khadija Hafidh

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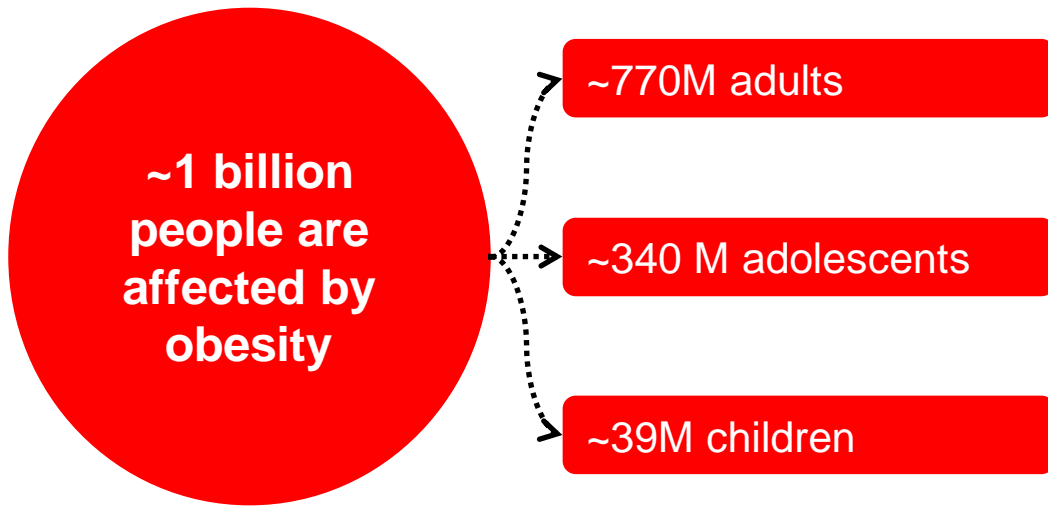


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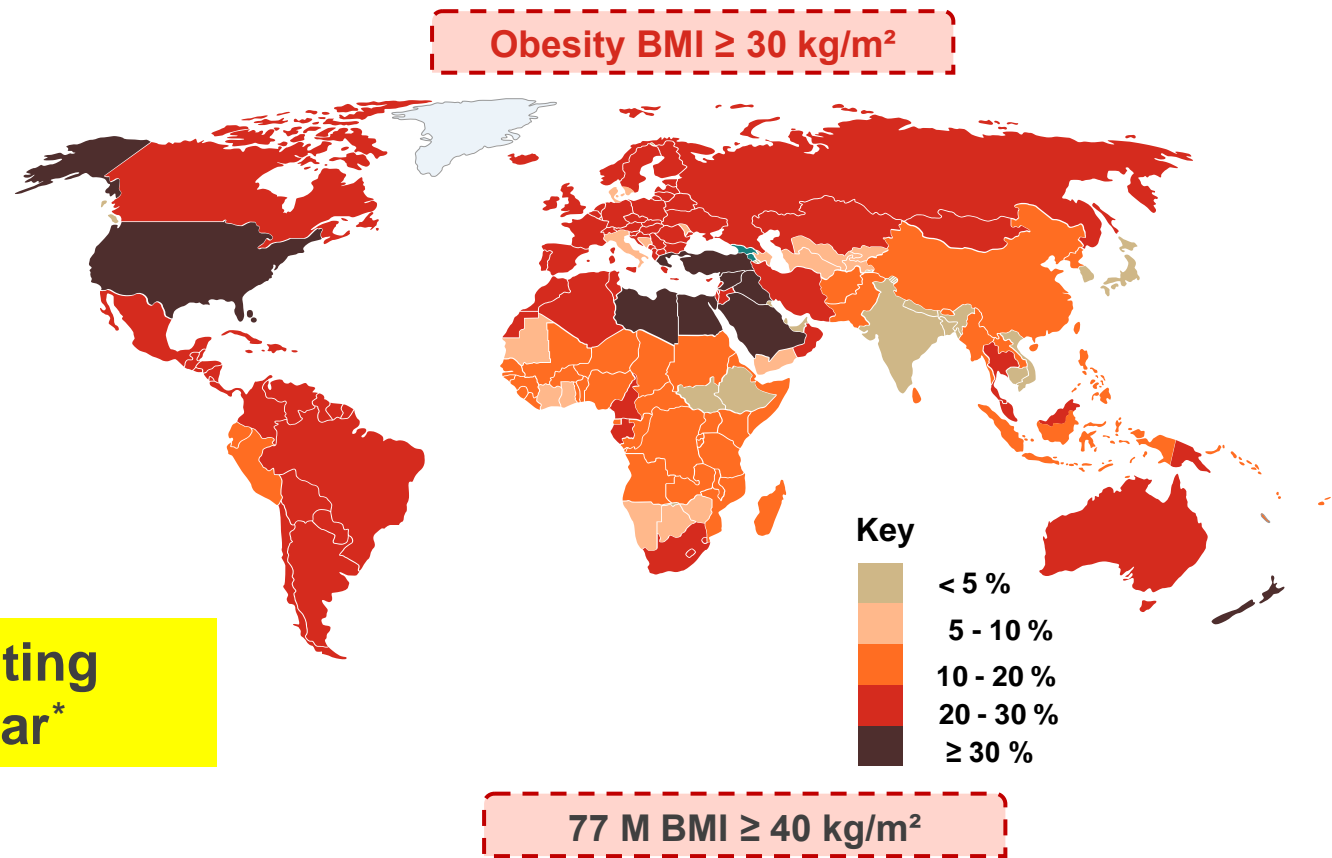
- ▶ Highlight Obesity Epidemiology
- ▶ Discuss the medical complications of Obesity
- ▶ Review Challenges in Obesity Management
- ▶ Discuss the role of GIP/GLP1 agonists in obesity management

Global prevalence of obesity

Obesity is a prevalent, complex, progressive and relapsing chronic disease, characterized by abnormal or excessive body fat (adiposity), **that impairs health**

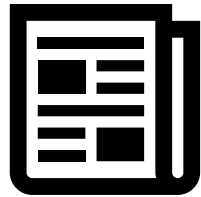


Obesity is associated with multiple life-limiting diseases and >4M premature deaths per year*



WHO key fact, Obesity and overweight, Jun 2021; WOF atlas 2022
*Why is the impact of obesity not being taken seriously? | World Economic Forum (weforum.org)

Definitions of Obesity



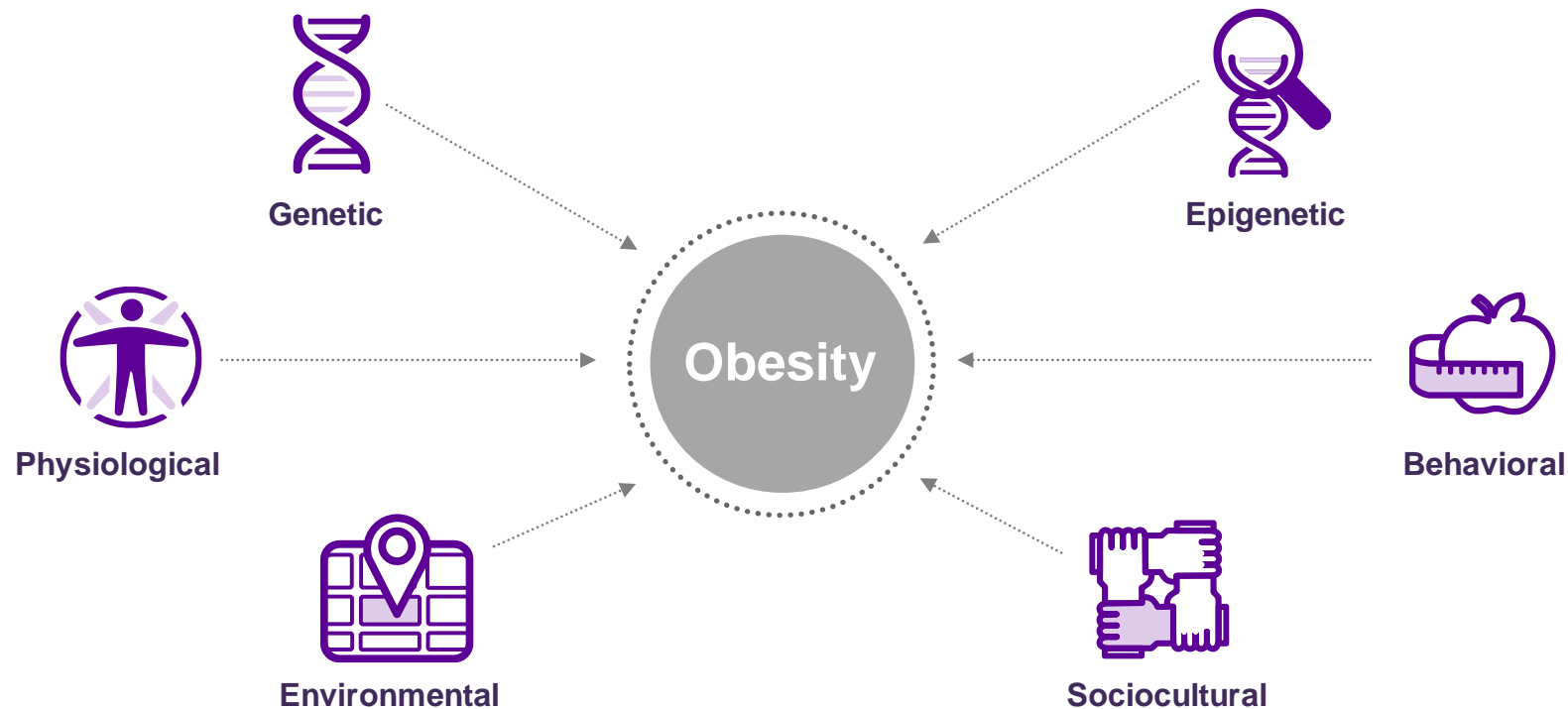
**Obesity in adults:
a clinical practice
guideline.**

CMAJ; 4 August 2020; Volume 192; Issue 31

***‘Obesity is a prevalent, complex,
progressive and
relapsing chronic disease,
characterised by abnormal or
excessive body fat (adiposity), **that**
impairs health.’***

Obesity is a chronic, progressive disease with origins that are often beyond an individual's control^{1,2}

The unbalanced energy consumption and expenditure seen in obesity are influenced by many factors^{1,3}:

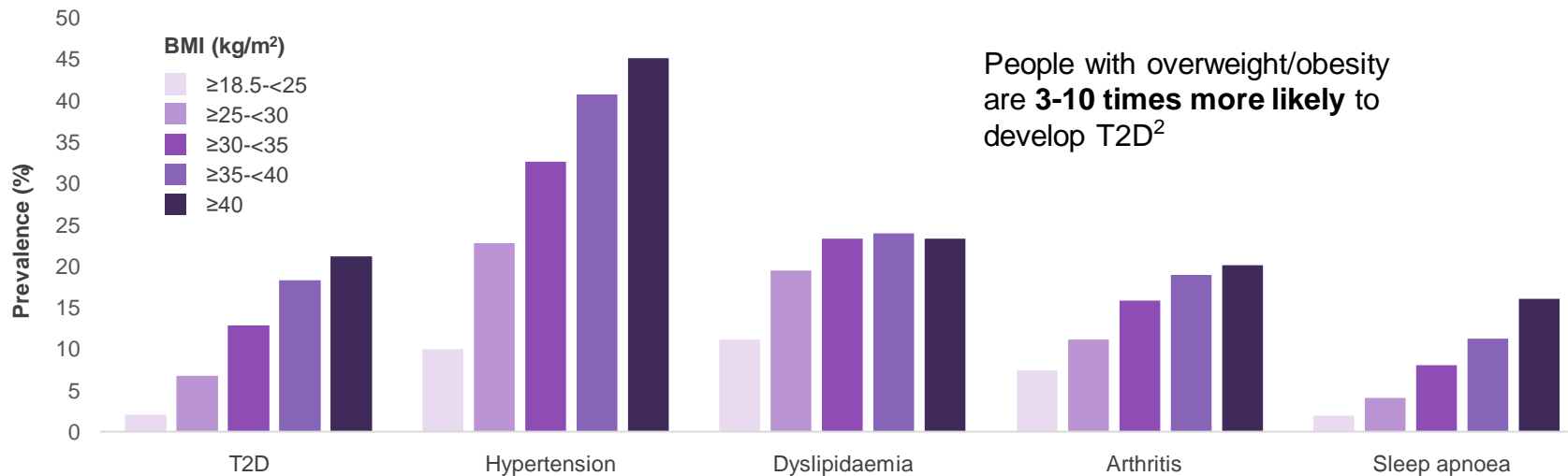


We need to approach the disease using multimodal therapy to achieve the best long-term treatment of obesity⁴

References: 1. Centers for Disease Control and Prevention. Accessed February 28, 2023. <https://www.cdc.gov/obesity/basics/causes.html> 2. Bray GA, et al. *Obes Rev.* 2017;18(7):715-723. doi:10.1111/obr.12551 3. Mahmoud AM. *Int J Mol Sci.* 2022;23(3):1341. doi:10.3390/ijms23031341 4. The Obesity Society. Accessed August 29, 2023. <https://www.prnewswire.com/news-releases/countrys-leading-obesity-care-organizations-develop-consensus-statement-on-obesity-301734250.html>

Obesity is a multisystem disease, putting people at increased risk for serious complications¹

Prevalence of Complications by BMI Category in 5 European Countries^{2a-c}



Other complications associated with a higher BMI include³⁻⁵:

- Anxiety and depression
- Kidney diseases
- Cardiovascular and nonalcoholic fatty liver diseases
- Musculoskeletal complications
- Certain cancers*

According to the European Society of Cardiology, obesity represents a major risk factor for coronary heart disease, including stable coronary artery disease, acute myocardial infarction, atrial fibrillation, and heart failure⁵

^aFrance, Germany, Italy, Spain, and the United Kingdom.²

^bAmong 58,364 respondents, 46.9% had BMI ≥18 kg/m² to <25 kg/m², 34.5% had BMI ≥25 kg/m² to <30 kg/m², 12.5% had BMI ≥30 kg/m² to <35 kg/m², 4.0% had BMI ≥35 kg/m² to <40 kg/m², and 2.1% had BMI ≥40 kg/m².²

^cp<0.05 compared with healthy weight in all 5 conditions.²

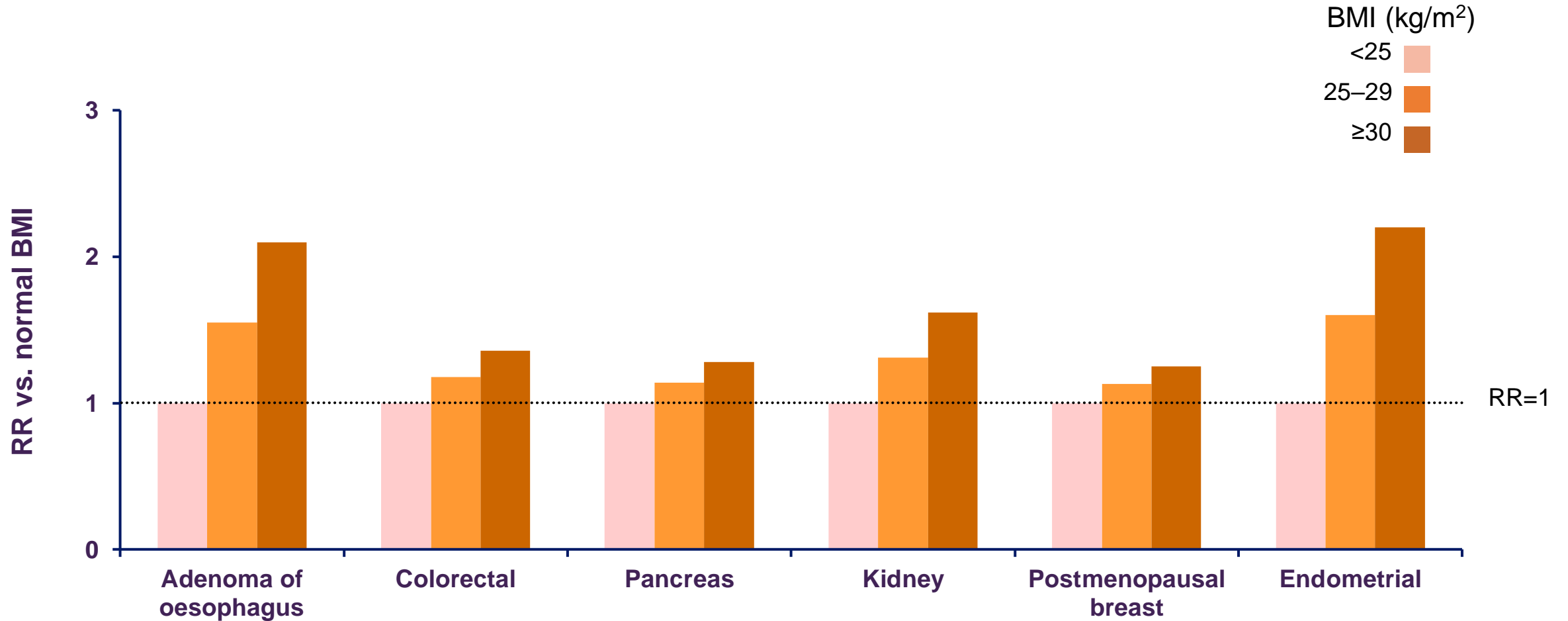
*Cancer types include adenocarcinoma of the oesophagus, meningioma, multiple myeloma, and cancer of the breast (in women who have gone through menopause), colon and rectum, uterus, gallbladder, upper stomach, kidneys, liver, ovaries, pancreas, and thyroid.³

References: 1. Sarma S, et al. *Diabetes Obes Metab.* 2021;23(suppl 1):3-16. doi:10.1111/dom.14290 2. Gupta S, et al. *Diabetes Metab Syndr Obes.* 2015;8:327-338. doi:10.2147/DMSO.S83696 3. Centers for Disease Control and Prevention.

Accessed March 10, 2023. <https://www.cdc.gov/cancer/obesity/index.htm> 4. Ansari S, et al. *Ther Adv Endocrinol Metab.* 2020;11:2042018820934955. doi:10.1177/2042018820934955 5. Badimon L, et al. *Eur Heart J.* 2017;38(25):1951-1958.

doi:10.1093/eurheartj/ehx181

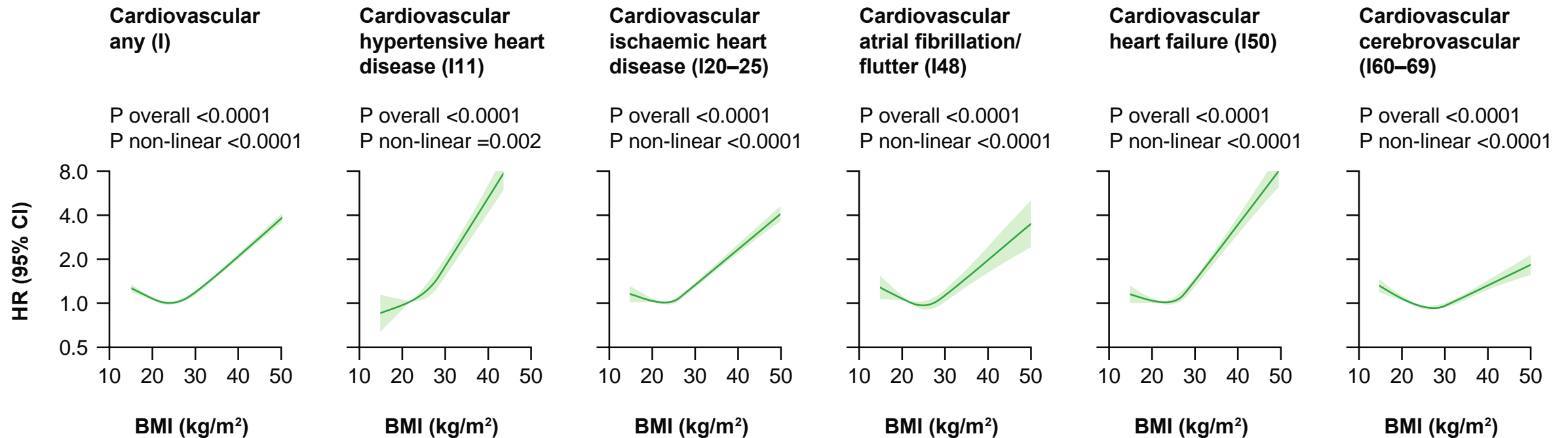
The risk of certain cancer increases with BMI



Data are summarized relative risk scores from a meta-analysis.
BMI=body mass index; RR=relative risk.
Modified from Ehemann C, et al. Cancer. 2012;118: 2338–2366.

Risk of cardiovascular disease increases as BMI increases

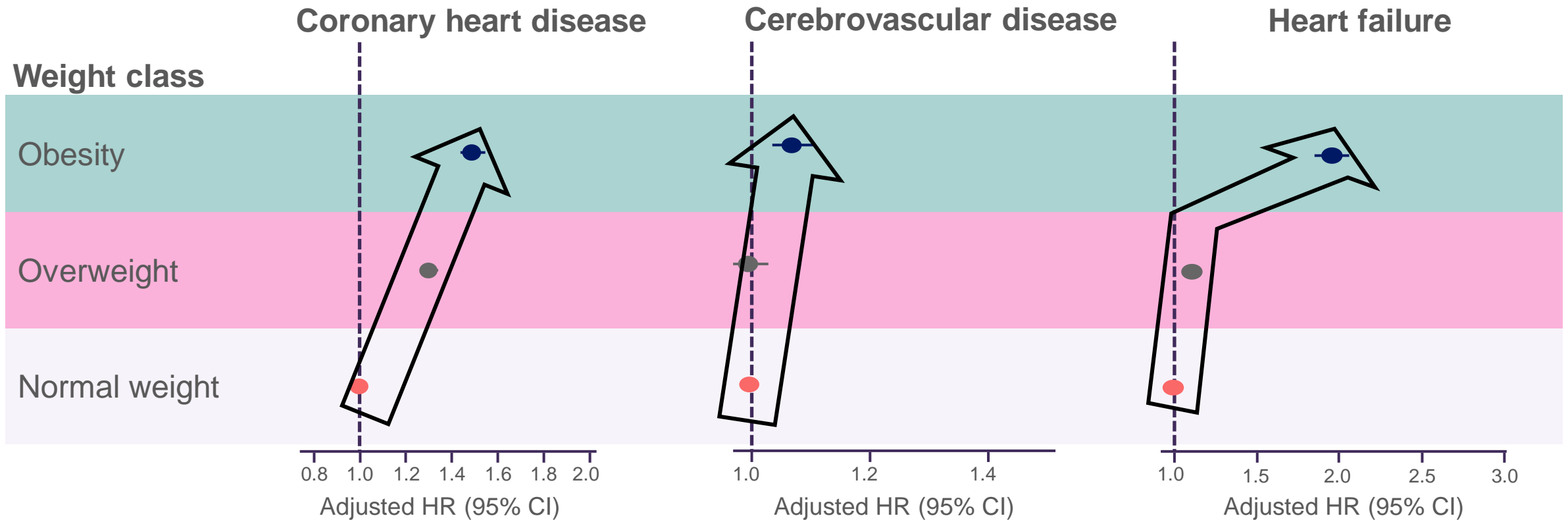
29% increased CVD risk for every 5 unit above BMI of 25 kg/m²



Population-based cohort study of 3.6 million adults in the UK

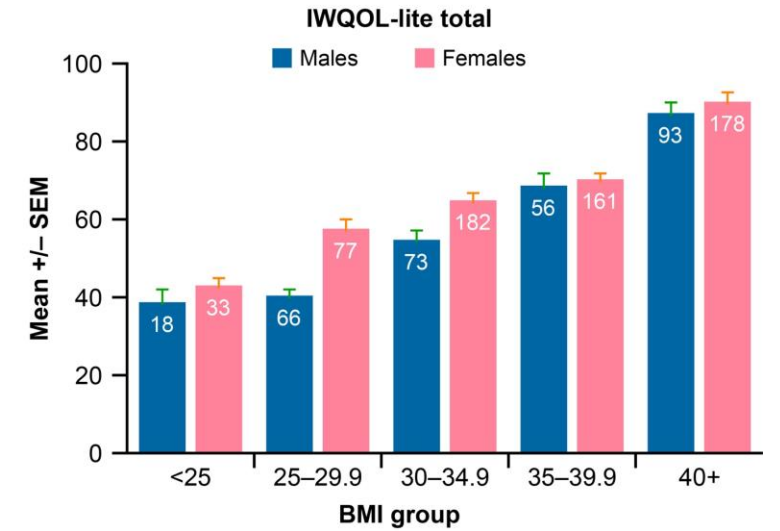
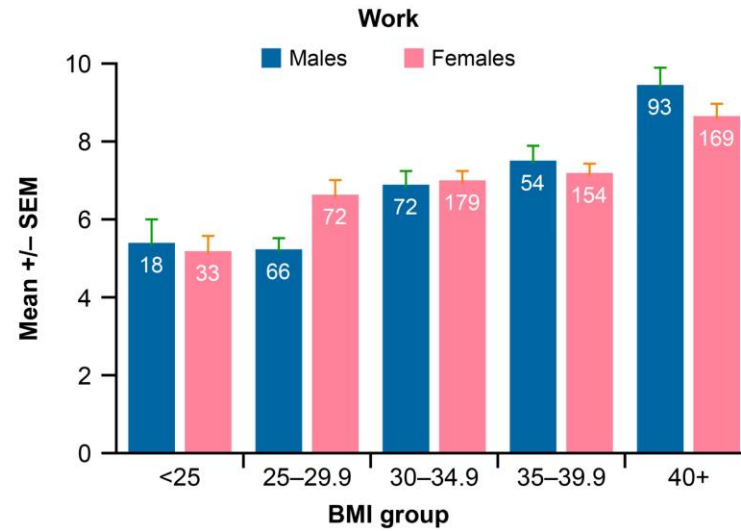
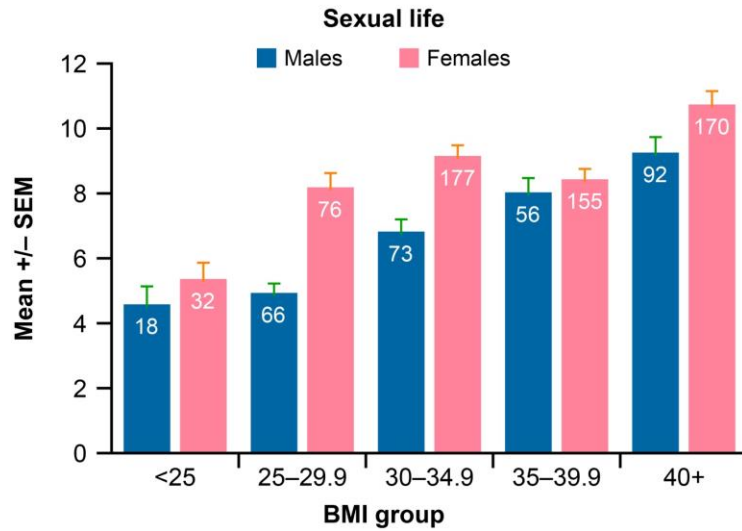
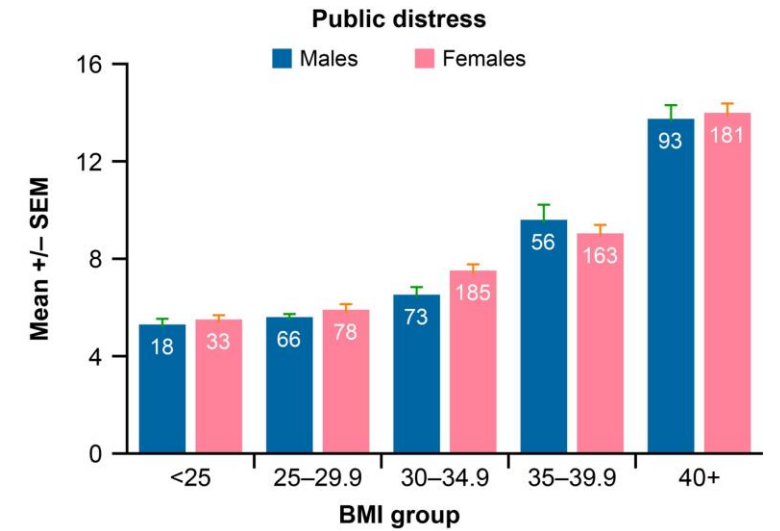
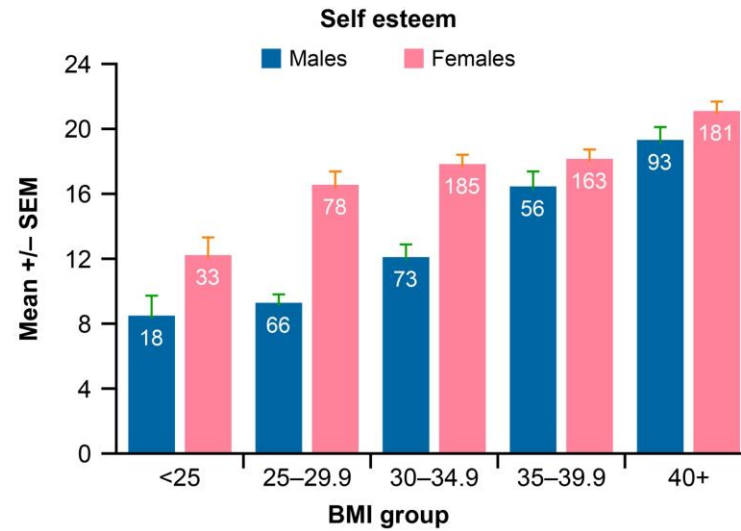
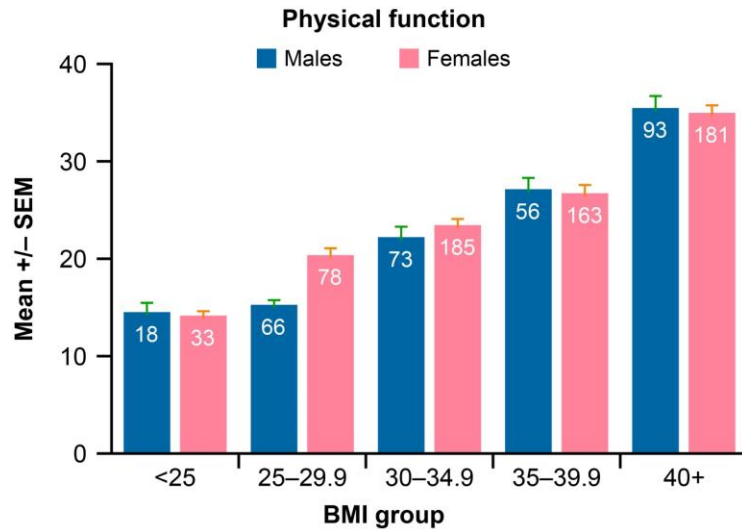
BMI=body mass index; CI=confidence interval; CVD=cardiovascular disease; HR=hazard ratio; UK=United Kingdom.
Modified from Bhaskaran K, Lancet Diabetes Endocrinol. 2018;6(12): 944-953.

Overweight and obesity increase the risk of CVD even in the absence of metabolic abnormalities



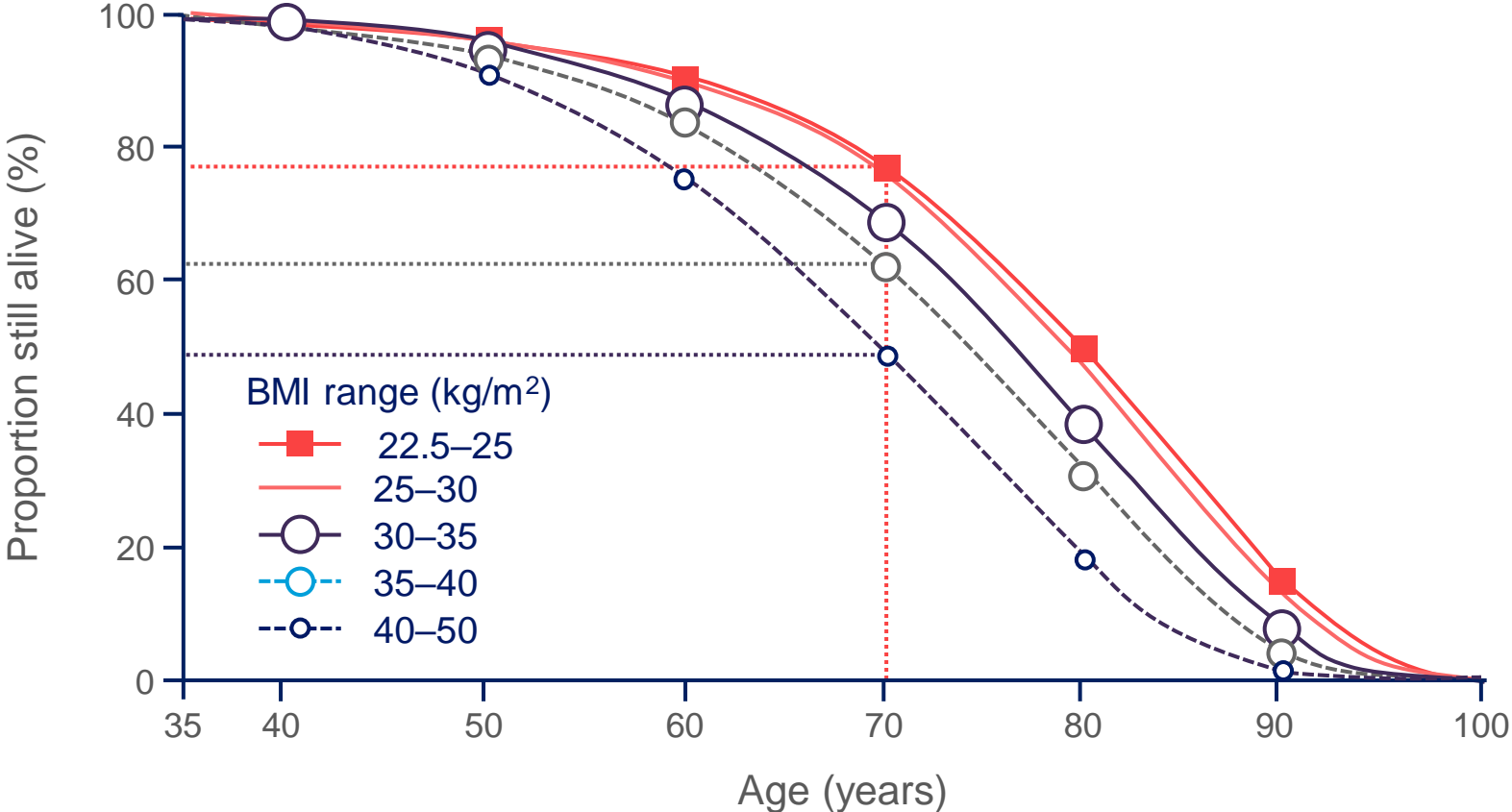
Body size, metabolic status and CVD events in 3.5 million UK adults. Analyses adjusted for age, sex, smoking status, and social deprivation. The reference category is normal weight, no metabolic abnormalities. CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; UK=United Kingdom. Modified from Caleyachetty R, et al. J Am Coll Cardiol. 2017;70(12): 1429–1437.

Impact of BMI on health-related quality of life



BMI=body mass index; IWQOL=Impact of Weight on Quality of Life; SEM=standard error of the mean.
 Modified from Kolotkin RL. Obesity Research, 2001;9(2): 102-111.

Life expectancy decreases as BMI increases



Normal BMI =
almost 80% chance of reaching
age 70

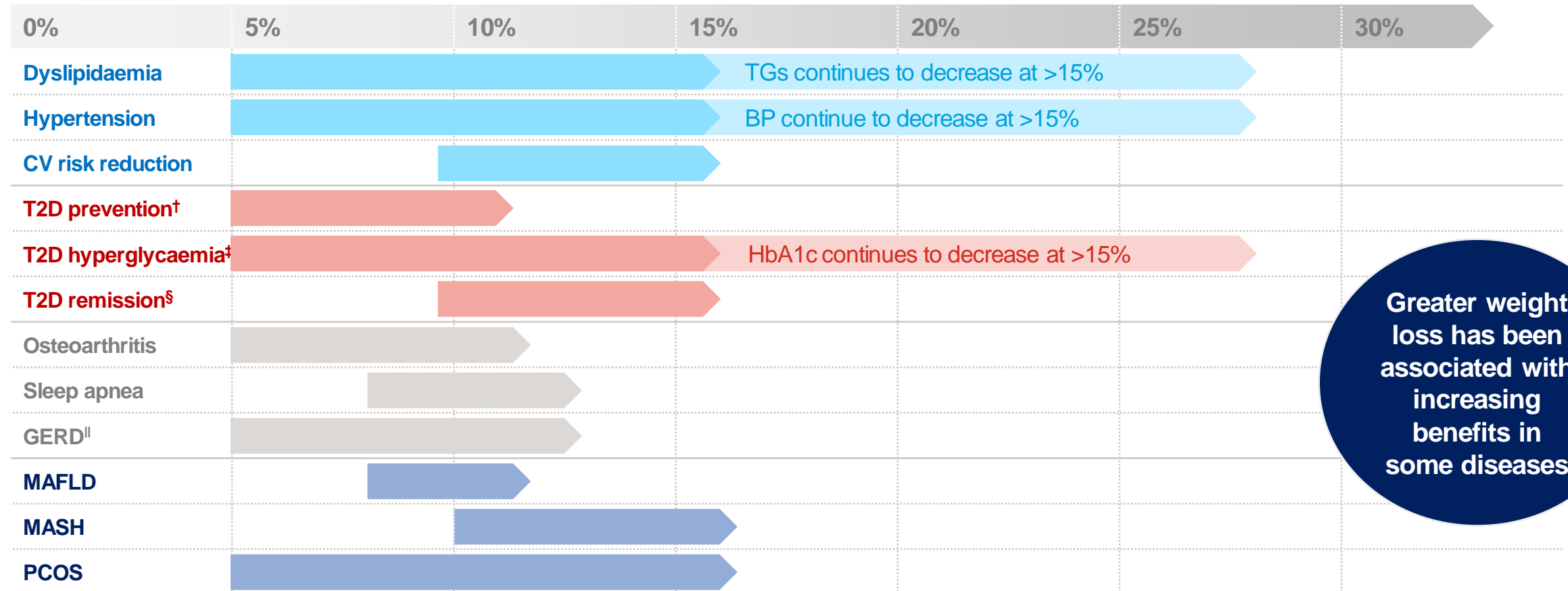
BMI 35–40 kg/m² =
~60% chance of
reaching age 70

BMI 40–50 kg/m² =
~50% chance of
reaching age 70

Data are based on male subjects; n=541,452.
BMI=body mass index.
Modified from Prospective Studies Collaboration. Lancet. 2009;373(9669): 1083–1096.

Weight loss can improve the complications of obesity¹⁻³

Percent Weight Loss

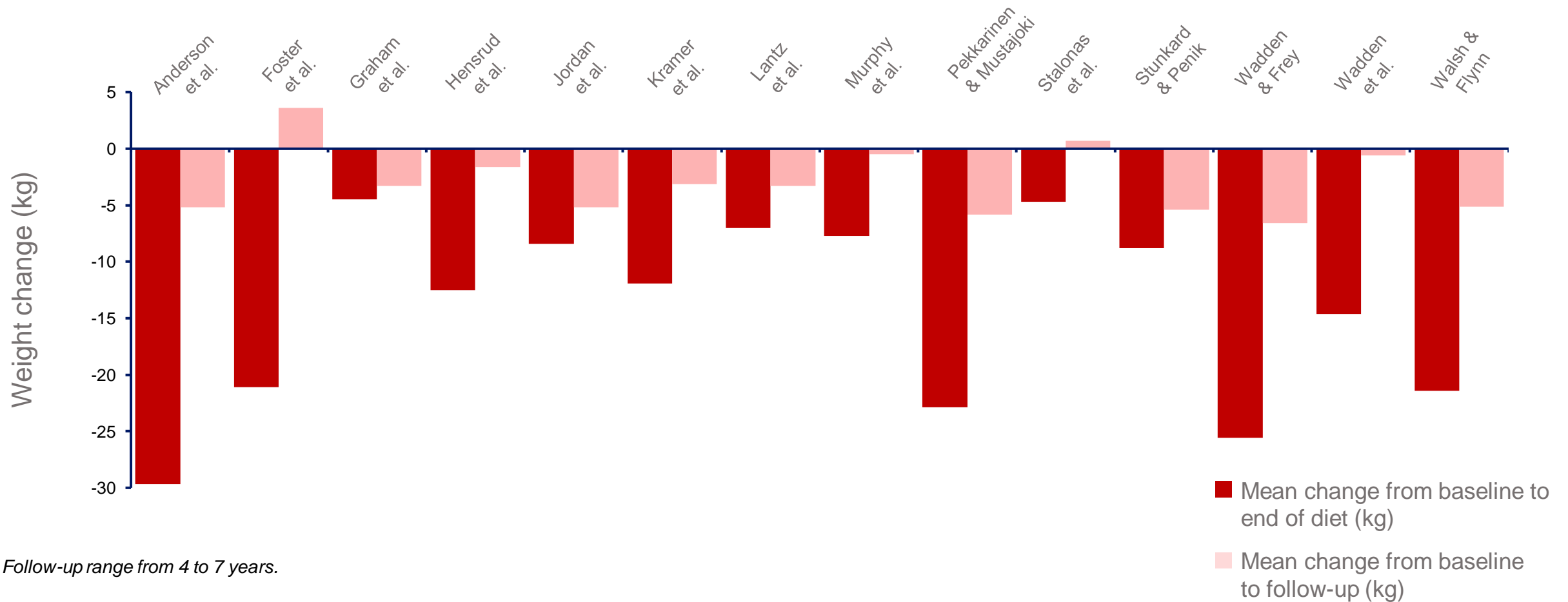


Greater weight loss has been associated with increasing benefits in some diseases

[§]Achieving HbA1c ≤6.5%. ^{||}Females 5%-10%; males 10%. BP=blood pressure; CV=cardiovascular; GERD=gastroesophageal reflux disease; HbA1c=glycated hemoglobin; MAFLD=Metabolic dysfunction- associated fatty liver disease; MASH=Metabolic dysfunction-associated steatohepatitis; PCOS=polycystic ovarian syndrome; T2D=type 2 diabetes; TG=triglycerides.

1. Cefalu WT, et al. *Diabetes Care*. 2015;38:1567-1582. 2. Horn DB, et al. *Postgrad Med*. 2022;134(4):359-375. 3. Garvey WT. *J Clin Endocrinol Metab*. 2022;107(4):e1339-e1347.

Maintenance of weight loss is challenging



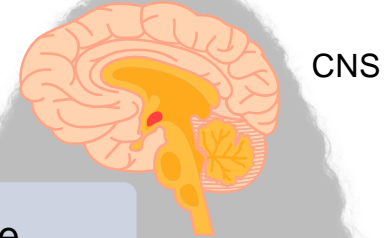
Follow-up range from 4 to 7 years.

Modified from Mann T, et al. Am Psychol. 2007;62(3): 220–233.

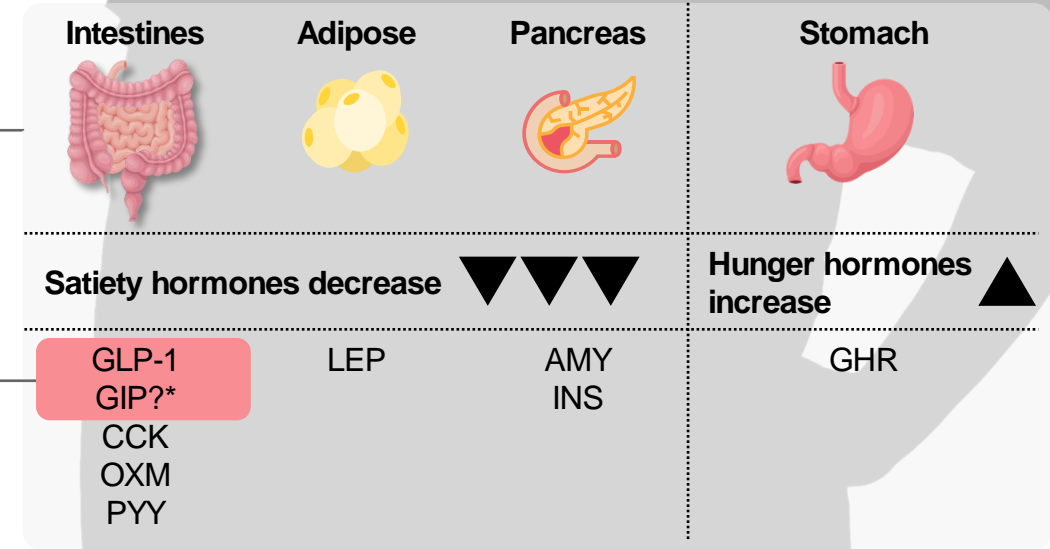
Why are patients with obesity struggling to lose weight and maintain weight loss?¹⁻⁵

When people with obesity reduce their weight, the body compensates by altering food intake and lowering energy expenditure associated with changes in a variety of hormones¹

Hormonal signals from adipose tissue, stomach, intestine, and the pancreas are communicated to the brain. These signals are integrated by the hypothalamus—the energy regulation command center—and **affect food intake and energy expenditure**³⁻⁵



Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) play a role in weight regulation³⁻⁵



*Though the role of GIP in satiety is supported by research, there are currently no data that support GIP levels decreasing with weight loss.
 AMY=amylin; CCK=cholecystokinin; CNS=central nervous system; GHR=ghrelin; INS=insulin; LEP=leptin; OXM=oxyntomodulin; PYY=peptide YY.
 1. Apovian CM, et al. *J Clin Endocrinol Metab.* 2015;100(2):342-362. 2. Hall KD, et al. *Med Clin North Am.* 2018;102(1):183-197.
 3. Melby CL, et al. *Nutrients.* 2017;9(5):468. 4. Samms RJ, et al. *Trends Endocrinol Metab.* 2020;31(6):410-421. 5. Roh E, et al. *Int J Mol Sci.* 2023;24(4):3384.

Most people with obesity do not reach target weight-loss goals with lifestyle interventions alone^{1*}



EASO Guidelines recommend **5%-15%** weight loss²
≥20% weight loss should be considered for people with BMI
≥35 kg/m²



Many people regain **50%** of their lost weight within 1-2
years³



▶ **AOMs** added to lifestyle intervention could fill the gap in treatment options available to achieve up to 15% weight loss in people with BMI ≥30-<35 kg/m² and with BMI ≥25-<30 kg/m² and comorbidities^{1,2}

Recognizing the importance of obesity treatment, countries including the United Kingdom and France provide reimbursement for newer AOMs^{4,5}

EASO=European Association for the Study of Obesity.

*Average weight loss <5%.¹

References: 1. Toplak H, et al. *Obes Facts*. 2015;8(3):166-174. doi:10.1159/000430801 2. Yumuk V, et al. *Obes Facts*. 2015;8(6):402-424. doi:10.1159/000442721 3. Kheniser K, et al. *J Clin Endocrinol Metab*. 2021;106(7):1854-1866.

doi:10.1210/clinem/dgab091

4. National Clinical Guideline Centre. Accessed February 6, 2023. <https://www.nice.org.uk/guidance/gid-ta10765/documents/final-appraisal-determination-document> 5. Haute Autorité de Santé. Accessed February 6, 2023.

https://www.has-sante.fr/jcms/p_3398698/fr/wegovy-semaglutide-obesite?portal=p_3058934

Guidelines recognize the value of AOMs as part of a comprehensive approach to weight loss



NICE guidelines recommend pharmacological interventions in conjunction with continued monitoring and adherence to lifestyle recommendations¹



EASO guidelines recommend pharmacotherapy combined with lifestyle interventions to help patients maintain compliance, manage obesity-related health risks, improve quality of life, and prevent the development of obesity-related comorbidities²



Canadian Obesity Clinical Practice Guidelines recommend that in addition to behaviour modification, pharmacotherapy for obesity management be considered early in the course of the disease, as weight and obesity-related health complications are likely to increase and progress with time³

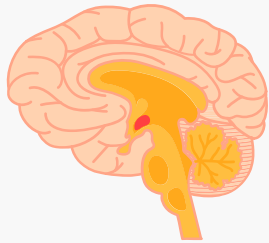


Obesity Ejadah recommendations 2024 for weight loss medication- should be prescribed in the long term as an adjunct to lifestyle modification. Pharmacotherapy for Obese Patients with BMI > 30 kg/m² with no comorbidities or BMI ≥ 27 kg/m² with co morbidities⁴

References: 1. National Institute for Health and Care Excellence. November 27, 2014. Accessed November 10, 2022. <https://www.nice.org.uk/guidance/cg189> 2. Toplak H, et al. *Obes Facts*. 2015;8(3):166-174. doi:10.1159/000430801 3. Pedersen SD, et al. Accessed January 31, 2023. <https://obesitycanada.ca/guidelines/pharmacotherapy> 4. Obesity Ejadah recommendations 2024

Proposed Roles of GIP and GLP-1 in Regulation of Metabolism^{1,2,*}

Brain



GIP activity*

↓ Reduced food intake

GLP-1 activity

↓ Reduced food intake

↑ Increased satiety

Subcutaneous white adipose tissue



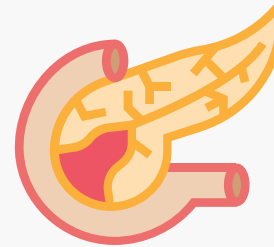
GIP activity*

↑ Increased insulin sensitivity

↑ Increased lipid-buffering capacity

↑ Increased storage capacity

Pancreas



GIP activity

↑ Increased insulin

↑ Increased glucagon in a glucose-dependent way

GLP-1 activity

↑ Increased insulin

↓ Reduced glucagon

Stomach



GLP-1 activity

↓ Reduced gastric emptying

*Demonstrated in preclinical research.

1. Samms RJ, et al. *Trends Endocrinol Metab.* 2020;31(6):410-421. 2. Roh E, et al. *Int J Mol Sci.* 2023;24(4):3384.

Introducing Mounjaro

A Once-Weekly, First-in-Class
GIP and GLP-1 Receptor Agonist

once weekly 
mounjaro[™]
(tirzepatide) injection

Lilly

Mounjaro Indications¹

Type 2 Diabetes Mellitus

Mounjaro is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

- ▶ as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- ▶ in addition to other medicinal products for the treatment of diabetes.

Weight Management

Mounjaro is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management, including weight loss and weight maintenance, in adults with an initial body mass index (BMI) of

- ▶ ≥ 30 kg/m² (obesity) or
- ▶ ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidaemia, obstructive sleep apnea, cardiovascular disease, prediabetes, or type 2 diabetes mellitus)

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE

Mounjaro Is a Single Molecule Designed to Activate Both the GIP and GLP-1 Receptors¹⁻³

| | |
|--------------------------|--|
| Structure | Based on the native GIP sequence ^{1,2} |
| Receptor activity | Activity on the GIP receptor is similar to the native GIP hormone, whereas activity of Mounjaro on the GLP-1 receptor is lower compared to the native GLP-1 hormone ² |
| Mean half-life | Approximately 5 days, enabling once-weekly dosing ³ |
| Dose adjustment | No dose adjustment of Mounjaro is recommended for patients with renal or hepatic impairment ² |

1. Willard FS, et al. *JCI Insight*. 2020;5(17):e140532.

2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

3. Coskun T, et al. *Mol Metab*. 2018;18:3-14.

How the GIP and GLP-1 Receptor Agonist Mounjaro Works¹⁻³



Activates the receptors of two naturally occurring hormones, GIP and GLP-1, **to reduce appetite and food intake, and increase fat utilization**^{1,2}



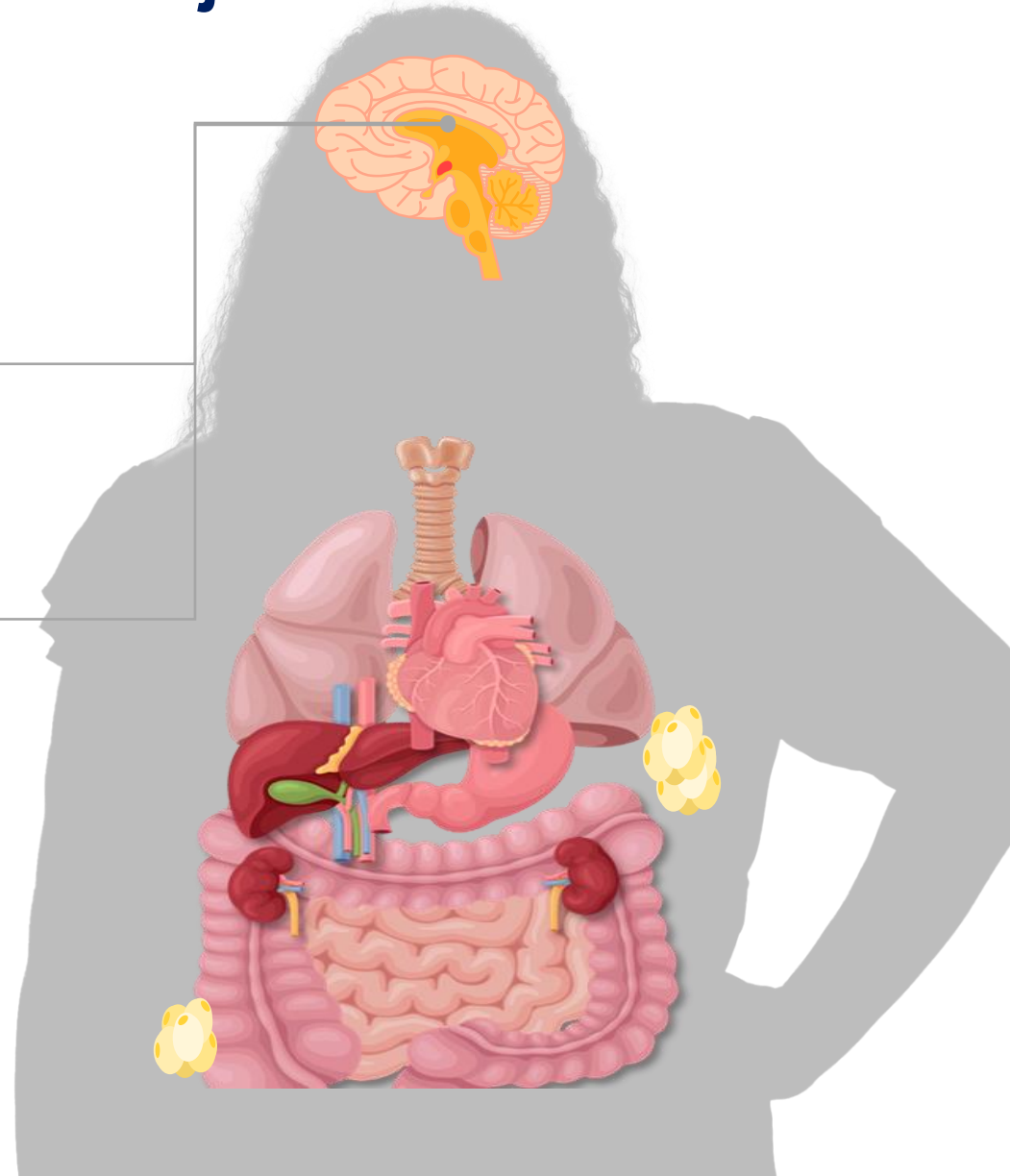
Reduces cravings for calorie-dense foods³



Increases feelings of satiety and **decreases** feelings of hunger¹



Lowers body fat mass, including visceral fat¹



1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.
2. Ravussin E, et al. *Diabetes*. 2023;72(1):127-OR. 3. Martin CK, et al. *Diabetes*. 2023;72(1):128-OR.

SURMOUNT Program

once weekly

mounjaro[™]
(tirzepatide) injection

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Mounjaro for Weight Management Is Being Evaluated in a Robust Clinical Trial Program¹⁻⁵

Overview of phase 3 trials assessing the efficacy and safety of Mounjaro*

| Trial | SURMOUNT-1 ¹ | SURMOUNT-2 ² | SURMOUNT-3 ³ | SURMOUNT-4 ⁴ | SURMOUNT-5 ⁵ |
|----------------------------|------------------------------------|--|--|--|------------------------------------|
| Comparator* | vs placebo (N=2539) | vs placebo (N=938) | vs placebo after an intensive lifestyle program (N=806) | vs placebo for maintenance of weight loss (N=783) | vs semaglutide 2.4 mg (N=700) |
| Patient population† | Adults with obesity or overweight‡ | Adults with obesity or overweight and T2D‡ | Adults with obesity or overweight‡ | Adults with obesity or overweight‡ | Adults with obesity or overweight‡ |
| Treatment period | 72 weeks | 72 weeks | 72 weeks | 88 weeks | 72 weeks |
| Completion date | April 2022 | April 2023 | May 2023 | May 2023 | December 2024 [§] |

Trials cannot be compared due to differences in study design, population, and key inclusion/exclusion criteria.

*All SURMOUNT trials are multicenter, double-blind, randomised, placebo-controlled, and QW administered. SURMOUNT-J and SURMOUNT-CN trials are not listed in this table as they are specific to Japan and China, respectively, and therefore not relevant to US payers. †All participants are adults 18 years or older with obesity (BMI ≥30 kg/m²), or overweight (BMI ≥27 kg/m²) with 1 or more weight-related complications. SURMOUNT-MMO participants are 40 years of age or older with established CVD or risk of CVD. ‡These studies included patients who reported ≥1 unsuccessful dietary effort to lose weight. §Estimated study completion date. †SURMOUNT-MMO's primary endpoint is a composite of any component event: all-cause death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and heart failure events.

QW=once weekly; TZP=tirzepatide.

1. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216 (and supplementary appendix). 2. SURMOUNT-2. ClinicalTrials.gov identifier: NCT04657003. Updated April 19, 2022. Accessed April 1, 2023. <https://clinicaltrials.gov/ct2/show/NCT04657003>. 3. SURMOUNT-3. ClinicalTrials.gov identifier: NCT04657016. Updated March 23, 2022. Accessed April 1, 2023. <https://clinicaltrials.gov/ct2/show/NCT04657016>. 4. SURMOUNT-4. ClinicalTrials.gov identifier: NCT04660643. Updated October 26, 2021. Accessed April 1, 2023. <https://clinicaltrials.gov/ct2/show/NCT04660643>. 5. SURMOUNT-5. ClinicalTrials.gov identifier: NCT05822830. Updated May 6, 2023. Accessed May 9, 2023. <https://clinicaltrials.gov/ct2/show/NCT05822830>

SURMOUNT-1

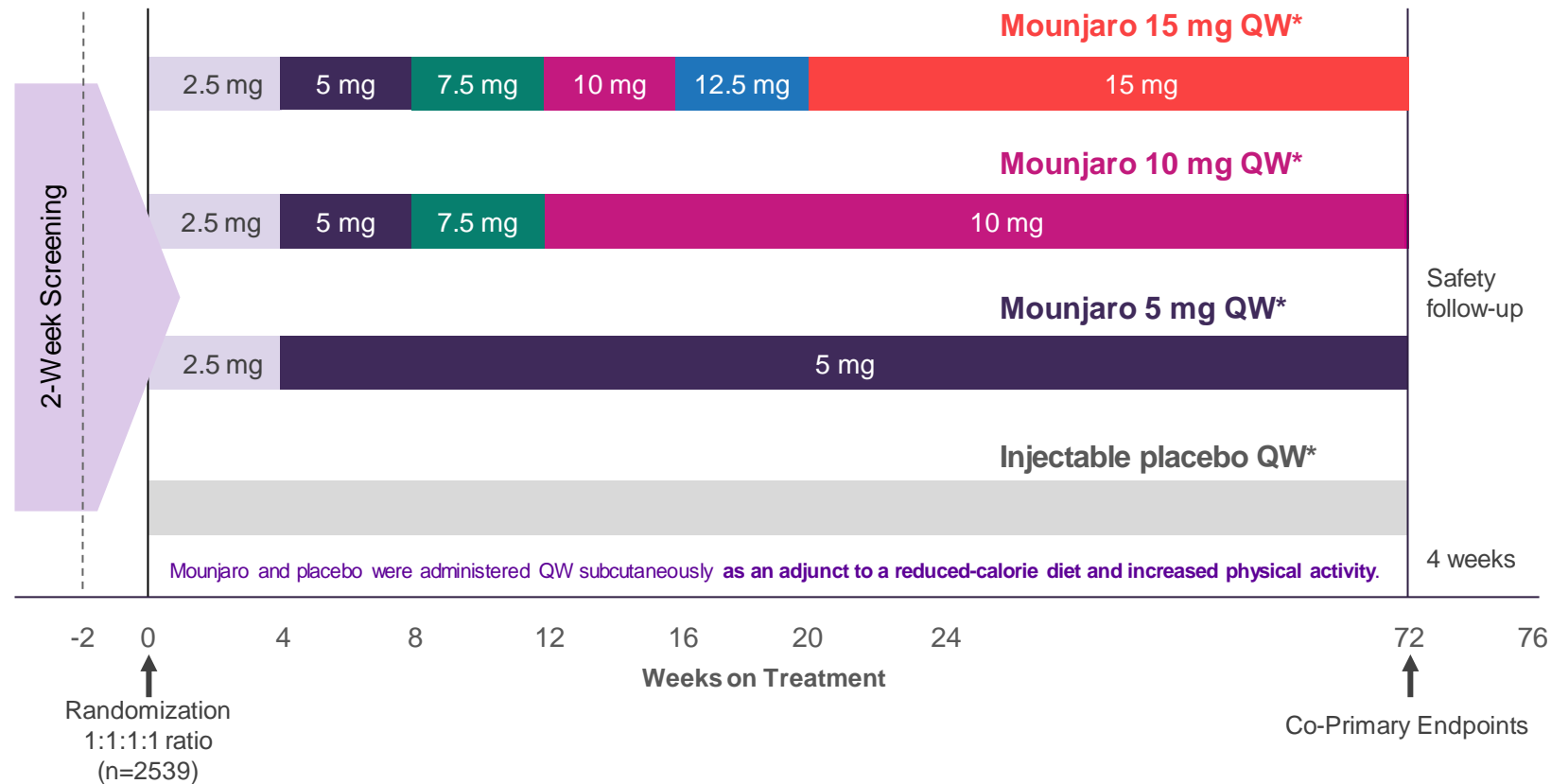
Mounjaro Once Weekly for the

Treatment of Patients With Obesity

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Mounjaro 5 mg, 10 mg, and 15 mg vs Placebo in Adults With Overweight or Obesity With Comorbidities, Excluding T2D^{1,2}



Brief Study Design

- SURMOUNT-1 included 2539 adults with a BMI of ≥ 30 kg/m² or a BMI of ≥ 27 kg/m² and at least 1 weight-related complication, excluding T2D
- Patients in all arms, including placebo, received instructions for a reduced-calorie diet and increased physical activity*

Co-Primary Endpoints (10 mg and/or 15 mg)

- Percentage change in weight from baseline at week 72
- Percentage of population with weight reduction of $\geq 5\%$ at week 72

Key Secondary Endpoints

- Systolic blood pressure, fasting insulin, and lipid levels (triglycerides, HDL cholesterol, non-HDL cholesterol) (all doses combined)
- Percentage of population with weight reduction of $\geq 10\%$, $\geq 15\%$, 20% at week 72 (10 mg and/or 15 mg)
- Change from baseline to week 72 in waist circumference (10 mg and/or 15 mg)
- Physical function score on the 36-Item Short Form Health Survey (SF-36), version 2, acute form (10 mg and 15 mg)
- Percentage change in body weight from baseline and percentage of population with weight reduction of $\geq 5\%$ at week 72 (5 mg)

Select Baseline Demographics^{1,2}

Averaged across treatment conditions (N=2539)

- Mean age=44.9 years
- Mean BMI=38.0 kg/m²
- Waist circumference=114.1 cm

*Included counselling by a dietitian or qualified healthcare professional, a deficit of 500 calories per day, and at least 150 minutes of physical activity per week.¹ Mounjaro and placebo were administered QW subcutaneously as an adjunct to a reduced-calorie diet and increased physical activity.¹

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Superior Weight Reductions With Mounjaro vs Placebo

once weekly

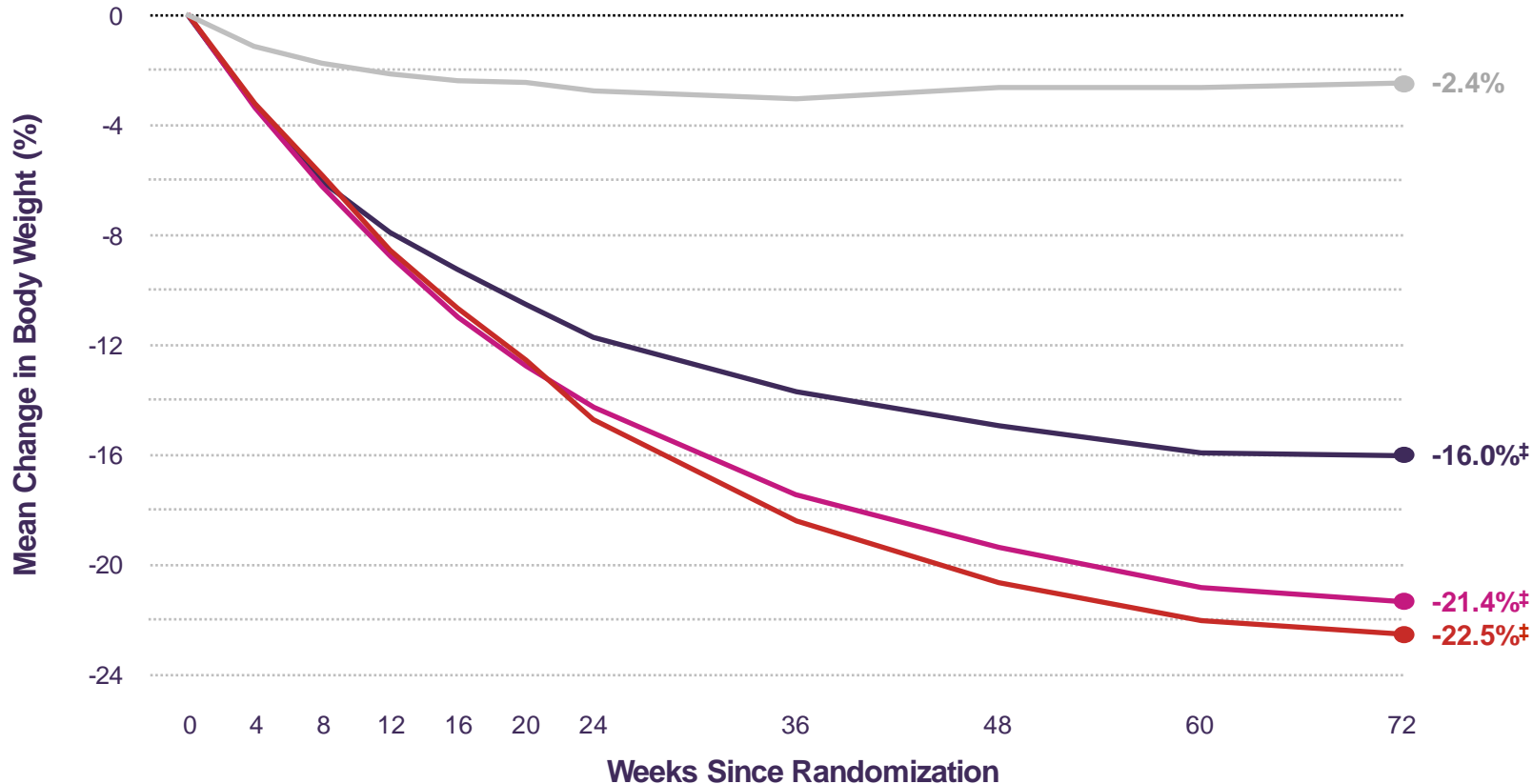
mounjaro[™]
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Results Seen as Early as 4 Weeks and Continued Through 72 Weeks With Mounjaro^{1,2,*}

Percentage Change in Body Weight Over Time From Baseline to Week 72*†

Mean baseline weight=104.8 kg



■ Injectable placebo (n=643) ■ Mounjaro 5 mg (n=630) ■ Mounjaro 10 mg (n=636) ■ Mounjaro 15 mg (n=630)

22.5%
average reduction
in body weight
with Mounjaro 15 mg
at 72 weeks‡

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² †Efficacy estimand, MMRM analysis, mITT population (efficacy analysis set).² ‡P<0.001 vs placebo, adjusted for multiplicity.²

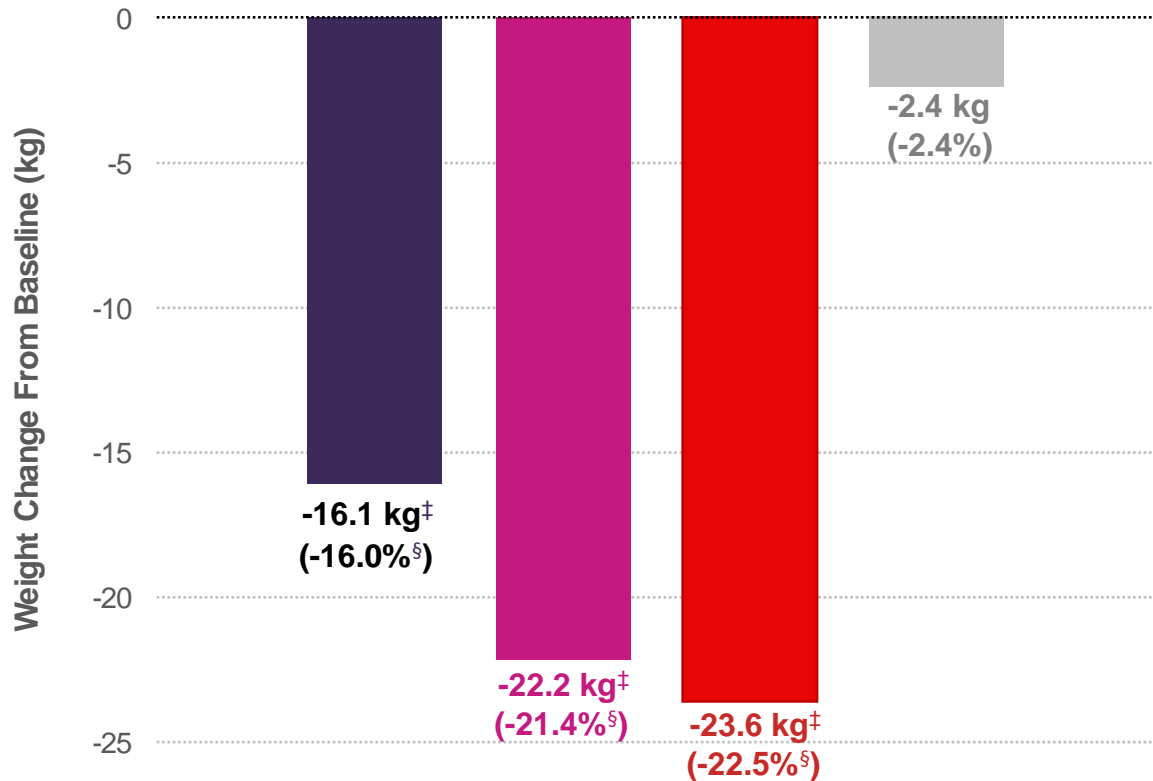
mITT=modified intention-to-treat;
MMRM=mixed model for repeated measures.

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Significant Weight Reductions With Mounjaro^{1,2,*}

Overall Change in Body Weight From Baseline at 72 Weeks^{*,†}

Mean baseline weight=104.8 kg



■ Injectable placebo (n=643) ■ Mounjaro 5 mg (n=630) ■ Mounjaro 10 mg (n=636) ■ Mounjaro 15 mg (n=630)

People taking Mounjaro 15 mg reduced their mean absolute body weight by an average of 23.6 kg at 72 weeks*

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² †Efficacy estimand, MMRM analysis, mITT population (efficacy analysis set).² ‡ $P < 0.001$ vs placebo, not adjusted for multiplicity.^{1,2} § $P < 0.001$ vs placebo, adjusted for multiplicity.^{1,2}

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Powerful Reductions in Body Weight With Mounjaro^{1,2,*}

Percentage of People Who Achieved $\geq 20\%$ and $\geq 25\%$ Weight Reduction at 72 Weeks^{*,†,‡}

Mean baseline weight=104.8 kg



More than 96% of people taking Mounjaro 10 mg and 15 mg demonstrated clinically significant weight loss of $\geq 5\%$ at 72 weeks^{*,†,‡, #}

~4 in 10
people taking
Mounjaro 15 mg
demonstrated
weight loss of $\geq 25\%$
at 72 weeks^{*,||}

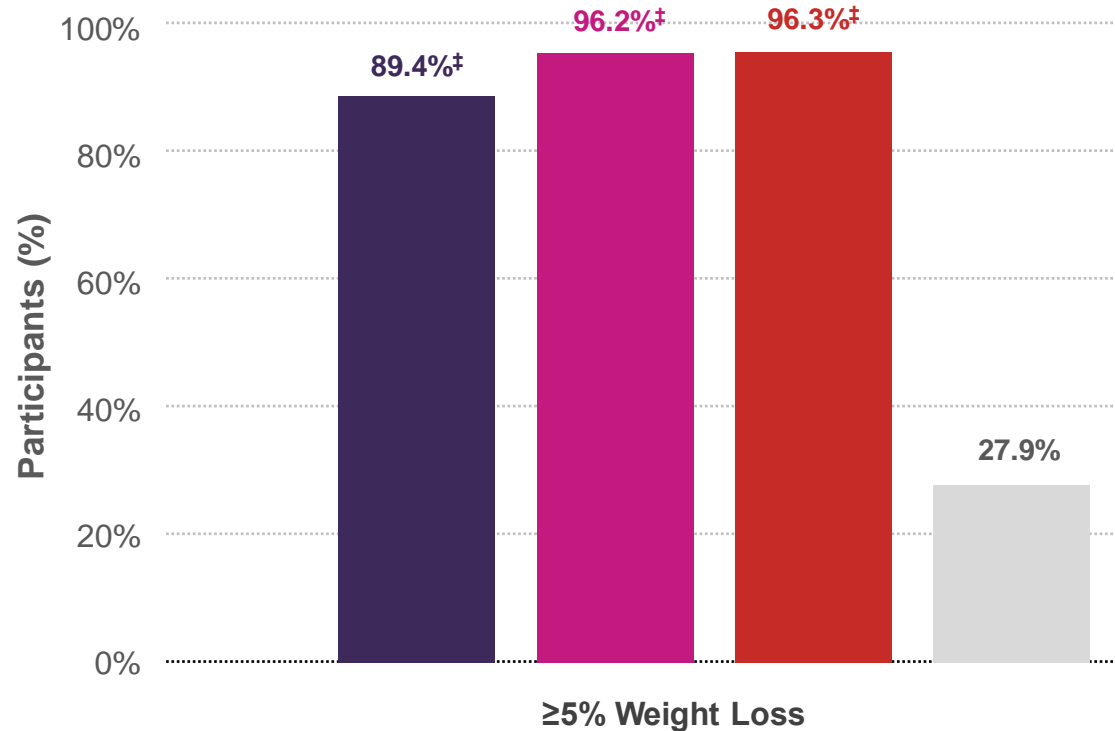
*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² †Efficacy estimand. ‡Logistic regression analysis. § $P < 0.001$ vs placebo, not adjusted for multiplicity. || $P < 0.001$ vs placebo, key secondary endpoint, adjusted for multiplicity. ¶Exploratory endpoint, hypothesis testing was not conducted. #Co-primary endpoint, adjusted for multiplicity.

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Proven Efficacy at Every Dose^{1,2,*}

Participants Who Met Weight-Reduction Targets From Baseline at Week 72^{*,†}

Mean baseline weight=104.8 kg



■ Injectible placebo (n=643) ■ Mounjaro 5 mg (n=630) ■ Mounjaro 10 mg (n=636) ■ Mounjaro 15 mg (n=630)

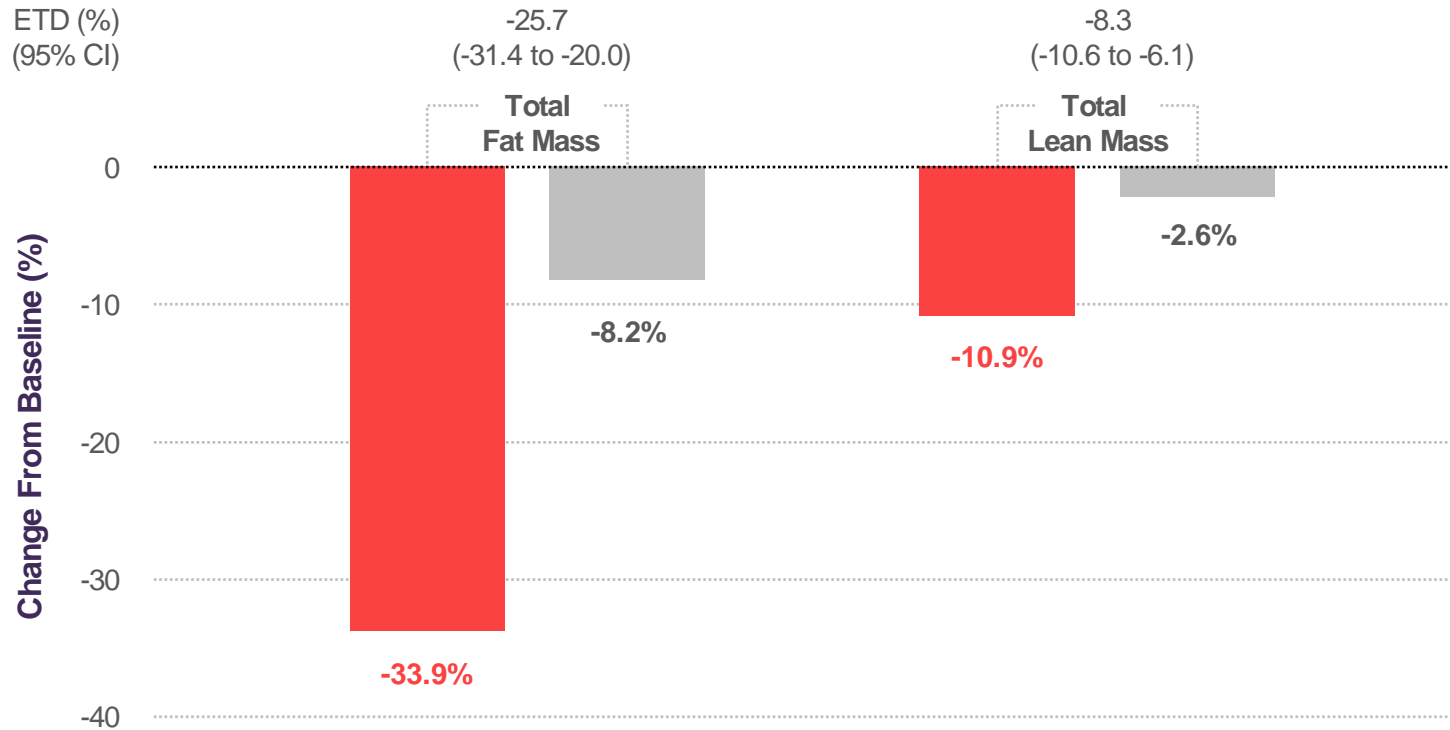
96%
of people taking
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≥5% at 72 weeks^{*,†}

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² [†]Co-primary endpoint for Mounjaro 10 mg and 15 mg. Efficacy estimand, logistic regression analysis. [‡] $P < 0.001$ vs placebo, adjusted for multiplicity.

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

People Taking Mounjaro Experienced Improvements in Body Composition^{1-3,*}

Percentage Change in Total Fat Mass and Total Lean Mass From Baseline at Week 72^{1,2,*}



In a subgroup of the SURMOUNT-1 clinical trial.¹

■ Pooled Mounjaro ■ Injectable placebo

Pooled Mounjaro groups and placebo (n=160)

Reduction in total fat mass was accompanied by a **reduction in visceral fat^{2,†}**

“Pooled Mounjaro” refers to pooled Mounjaro 5-mg, 10-mg, and 15-mg groups, unless otherwise indicated.

The percentage change in total body fat mass from baseline to week 72 was assessed in a subset of participants who underwent DXA (n=255 enrolled; n=160 completers with both baseline and week 72 DXA).^{1,2}

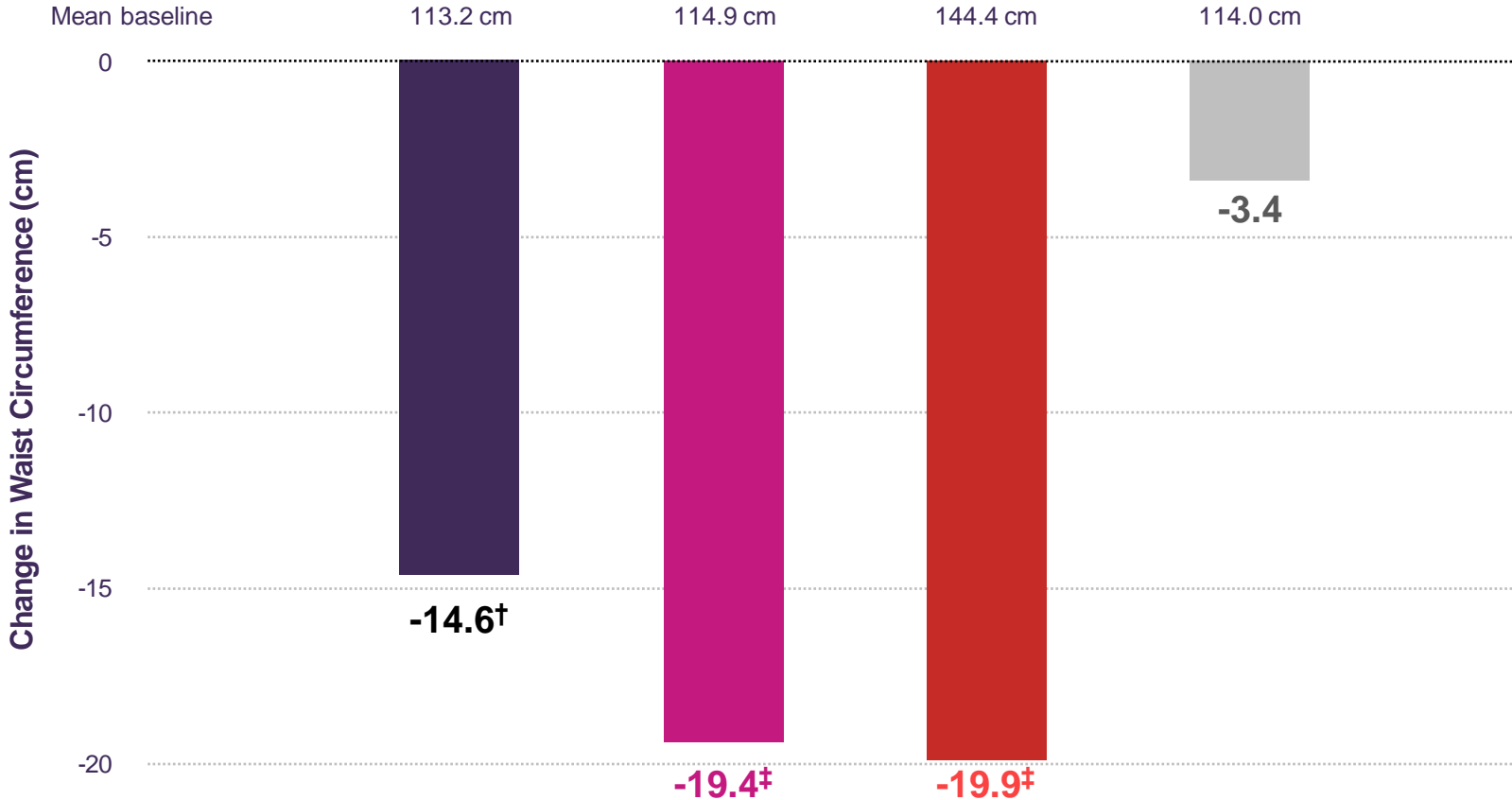
*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.¹ †Visceral fat and its accumulation are risk factors for metabolic diseases.³

CI=confidence interval; DXA=dual x-ray absorptiometry; ETD=estimated treatment difference.

1. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix). 2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 3. Samms RJ, et al. *Trends Endocrinol Metab.* 2020;31(6):410-421.

People Taking Mounjaro 15 mg Experienced a 19.9-cm Reduction in Waist Circumference at 72 Weeks^{1,2,*}

Mean Reduction in Waist Circumference From Baseline to 72 Weeks^{1,*}



- Mounjaro 5 mg (n=630)
- Mounjaro 10 mg (n=636)
- Mounjaro 15 mg (n=630)
- Injectable placebo (n=643)

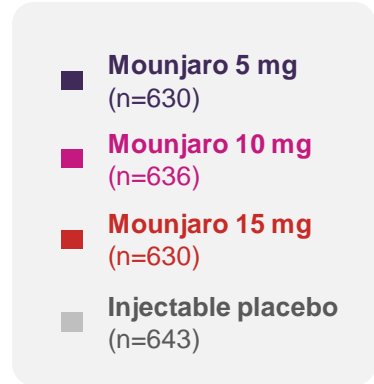
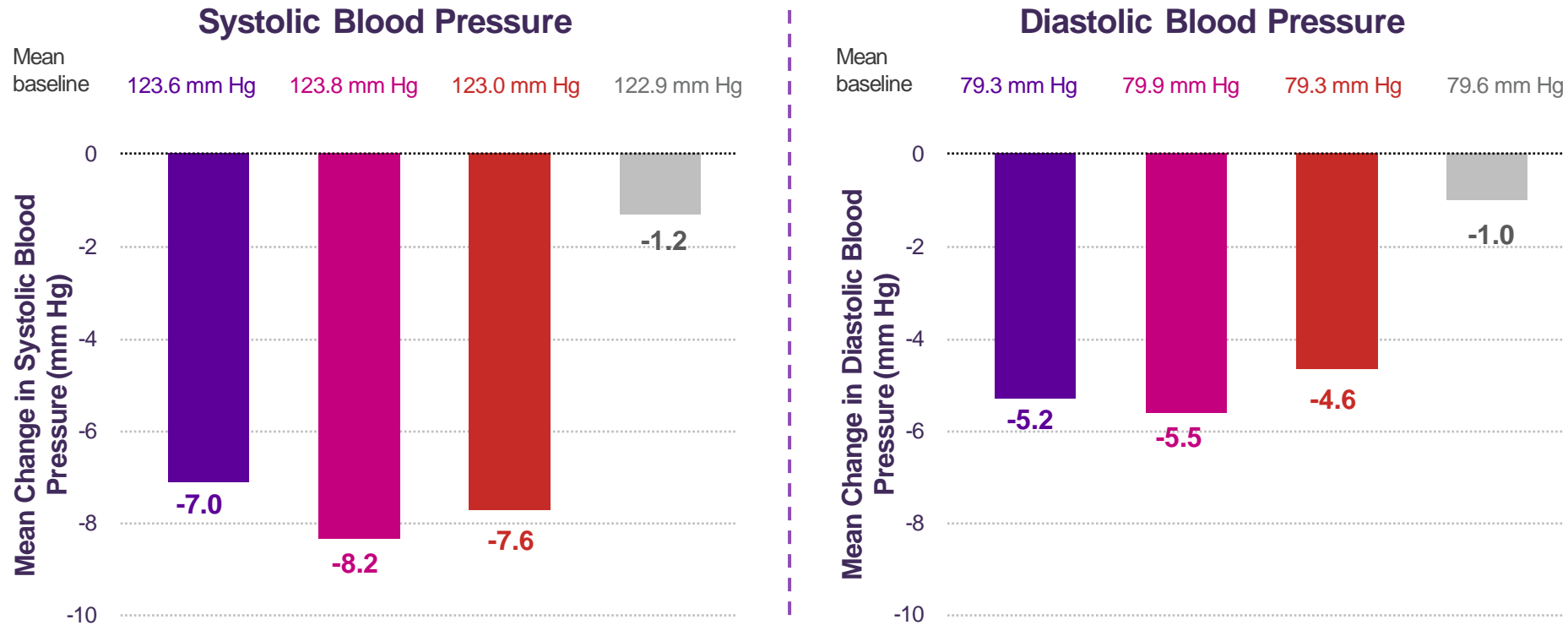
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1. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix). 2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

Changes in Systolic and Diastolic Blood Pressure in SURMOUNT-1 at 72 Weeks in People Taking Mounjaro^{1,2,*}

Mean Reduction in Blood Pressure From Baseline to 72 Weeks (mm Hg)^{1,*}

EFFICACY ESTIMAND NOT ADJUSTED FOR MULTIPLICITY

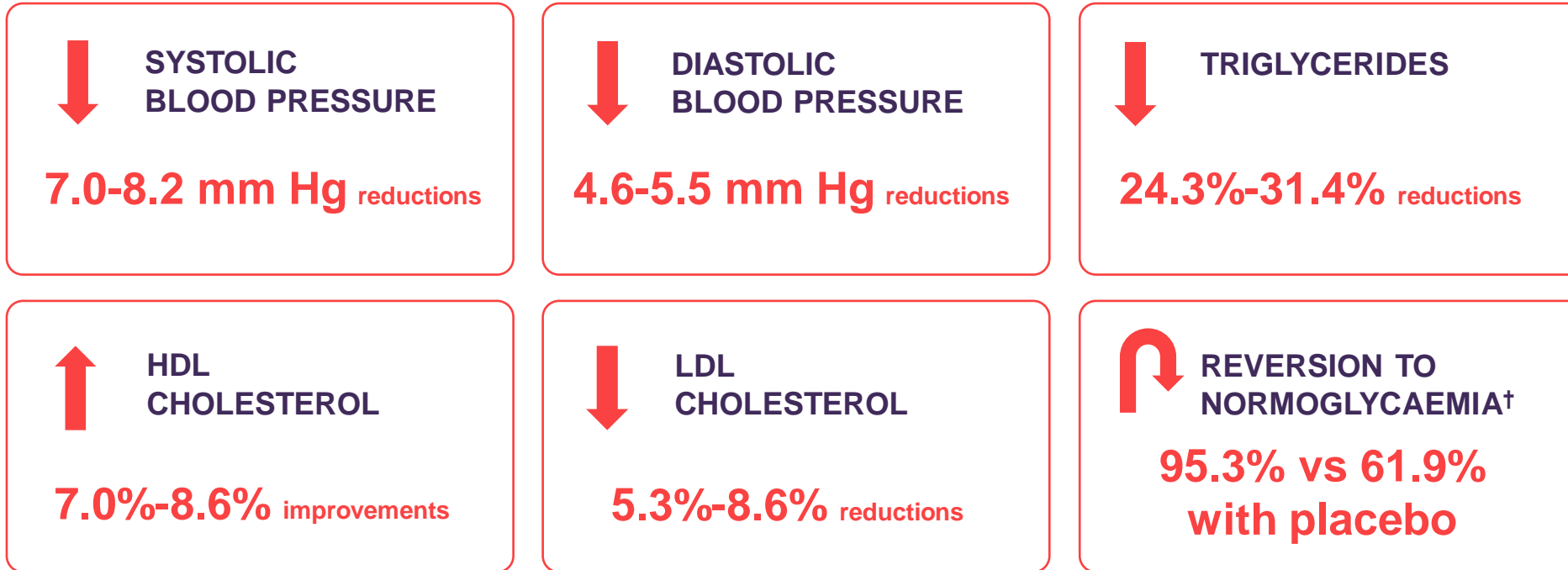


*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.¹

1. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216. 2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

Mounjaro is indicated for chronic weight management and T2DM in adults and is NOT indicated for any cardiometabolic diseases including hypertension, hypertriglyceridemia or dyslipidemia.

People Taking Mounjaro Experienced Improvements in Cardiometabolic Parameters at 72 Weeks^{1,2,*}



Mounjaro is indicated for chronic weight management and T2DM in adults and is NOT indicated for any cardiometabolic diseases including hypertension, hypertriglyceridemia or dyslipidemia.

Mounjaro 5 mg: n=630
Mounjaro 10 mg: n=636
Mounjaro 15 mg: n=630
Placebo: n=643

Observed in the SURMOUNT-1 phase 3 clinical trial of Mounjaro (5 mg, 10 mg, and 15 mg) vs placebo. These are ranges from averages by each dosage group.^{1,‡}

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.¹ [†]Reversion percentages of people who had prediabetes at baseline. Prediabetes defined as fasting glucose obtained alone or at time = 0 min during a 2-hour oral glucose tolerance test (OGTT) of 100-125 mg/dL (5.6-6.9 mmol/L), 2-hour glucose obtained at time = 120 min during an OGTT 140-199 mg/dL (7.8-11.0 mmol/L), and HbA1c of 5.7%-6.4% (39-47 mmol/mol). At least 2 abnormal tests were required to diagnose prediabetes. [‡]Averages from each dosage group are the least-squares mean change from baseline. Statistical tests were done for each dosage group, not the ranges from group means. The efficacy estimand for individual doses was not adjusted for multiplicity.¹

HDL=high-density lipoprotein; LDL=low-density lipoprotein.

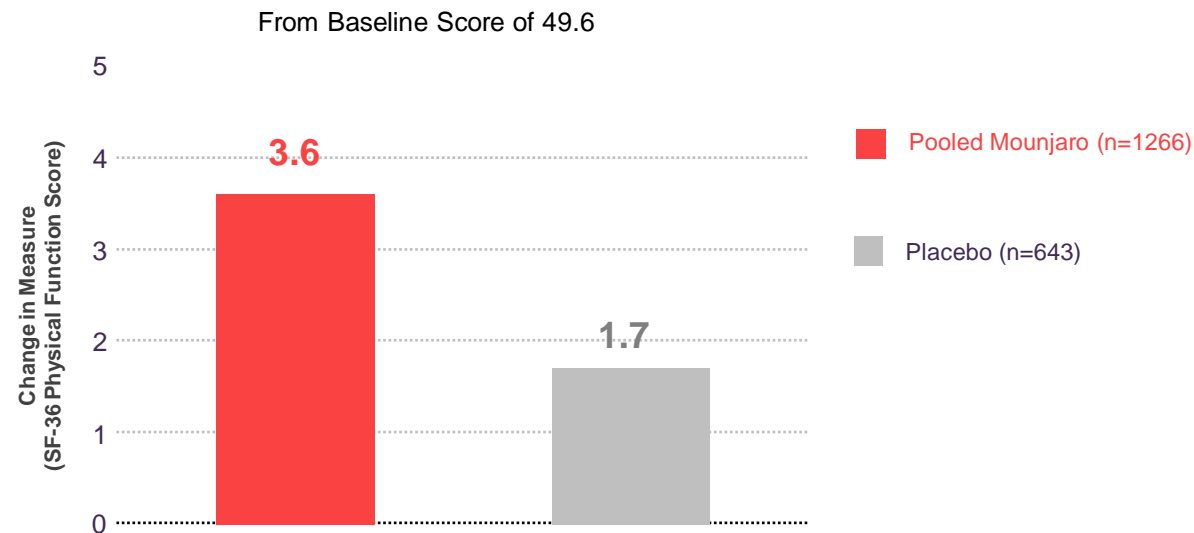
1. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

People Taking Mounjaro Experienced Improvement in Physical Functioning and Health-Related Quality of Life^{1-3,*}

In SURMOUNT-1, people taking Mounjaro experienced improvement in physical functioning score vs placebo^{*,†}

Mean Change in SF-36v2 Physical Function Score at Week 72 (%)*,†,‡



Improvement was assessed using the **36-Item Short Form Health Survey (SF-36), version 2, acute form**, a widely used questionnaire that evaluates **functional health and well-being**

Some of the key measures included:

- ▶ Physical functioning
- ▶ Bodily pain
- ▶ Vitality
- ▶ Mental health
- ▶ General health

Data are for the pooled 10-mg and 15-mg tirzepatide groups.

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related comorbidity, excluding type 2 diabetes.^{2,3} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² † $P < 0.001$ compared to placebo, adjusted for multiplicity. Treatment regimen estimand, ANCOVA model. ‡Change from baseline for SF-36 was assessed using ANCOVA model with terms for baseline SF-36 physical function score, treatment, and stratification factors that included an assessment of personal limitations due to physical and psychological problems, vitality (energy and fatigue), bodily pain, mental health, and perception of overall health.

ANCOVA=analysis of covariance.

1. Palao-Ocharan P, et al. *Orphanet J Rare Dis.* 2022;17(88). 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix). 3. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

What Could the SURMOUNT-1 Data Mean for Patients Living with Obesity?

If a patient takes Mounjaro in addition to a reduced-calorie diet and increased physical activity, she/he could potentially^{1,2}

- ▶ **Achieve** significant and sustained weight loss, up to an average of **23.6 kg (22.5%)***
- ▶ **Experience** improvement in her/his cardiometabolic profile

*Data for Mounjaro 15-mg dose vs -2.4% (-3 kg) for placebo in a 72-week study, in addition to a reduced-calorie diet and increased physical activity.

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Mounjaro is indicated for chronic weight management and T2DM in adults and is NOT indicated for any cardiometabolic diseases including hypertension, hypertriglyceridemia or dyslipidemia.

Safety

once weekly 
mounjaro[™]
(tirzepatide) injection

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Adverse Reactions in the SURMOUNT-1 Clinical Trial^{1,2,*}

Mounjaro has a similar safety profile to other incretin-based therapies

- ▶ **The most common adverse reactions** were gastrointestinal in nature and were mostly mild to moderate
- ▶ Gastrointestinal adverse reactions primarily **occurred during dose escalation and decreased over time**

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.² †All participants in the clinical trial received Mounjaro with an autoinjector pen.

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216 (and supplementary appendix).

| Adverse Reactions Reported in People Taking Mounjaro* | | | | |
|---|--------------------------|---------------------------|---------------------------|--------------------|
| | Mounjaro 5 mg (n=630) | Mounjaro 10 mg (n=636) | Mounjaro 15 mg (n=630) | Placebo (n=643) |
| Nausea | 24.6% | 33.3% | 31.0% | 9.5% |
| Diarrhea | 18.7% | 21.2% | 23.0% | 7.3% |
| Constipation | 16.8% | 17.1% | 11.7% | 5.8% |
| Dyspepsia | 8.9% | 9.7% | 11.3% | 4.2% |
| Vomiting | 8.3% | 10.7% | 12.2% | 1.7% |
| Decreased appetite | 9.4% | 11.5% | 8.6% | 3.3% |
| Headache | 6.5% | 6.8% | 6.5% | 6.5% |
| Abdominal pain | 4.9% | 5.3% | 4.9% | 3.3% |
| Hair loss | 5.1% | 4.9% | 5.7% | 0.9% |
| Dizziness | 4.1% | 5.5% | 4.1% | 2.3% |
| Eructation | 3.8% | 5.2% | 5.6% | 0.6% |
| Injection site reaction† | 2.9% | 5.7% | 4.6% | 0.3% |

Discontinuation Due to Adverse Reactions^{1,2,*}

| Percentage of People Who Discontinued Treatment* | | | | |
|---|--------------------------|---------------------------|---------------------------|--------------------|
| | Mounjaro 5 mg (n=630) | Mounjaro 10 mg (n=636) | Mounjaro 15 mg (n=630) | Placebo (n=643) |
| Discontinuation due to adverse reactions | 4.3% | 7.1% | 6.2% | 2.6% |
| Discontinuation due to gastrointestinal adverse reactions | 1.3% | 2.8% | 2.9% | 0.3% |

- ▶ The most common adverse reactions were gastrointestinal in nature and were mostly mild to moderate
- ▶ Gastrointestinal adverse reactions primarily occurred during dose escalation and decreased over time

*Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.²

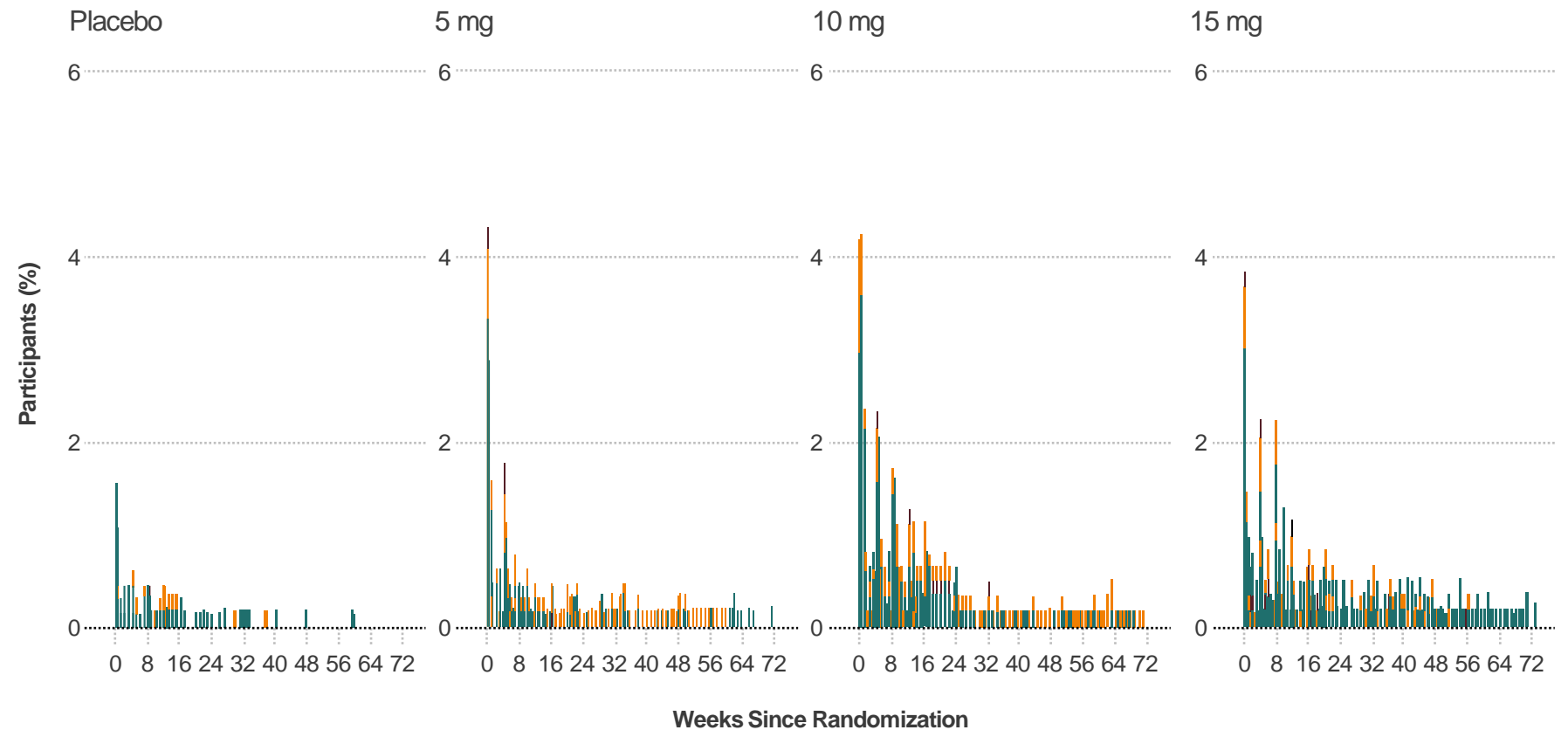
1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 2. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216 (and supplementary appendix).

Incidence of Nausea Over Time^{1,2,*}

- ▶ Most gastrointestinal events—including nausea, vomiting, and diarrhea—**were transient, occurring primarily during the dose-escalation period,** and were mostly mild to moderate in severity*

Nausea severity

- Mild
- Moderate
- Severe



*Percentages are based on the number of participants at risk at specific observation times. Studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{1,2} All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.¹

1. Jastreboff AM, et al. *N Engl J Med.* 2022;387(3):205-216.

2. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

Key Takeaways¹⁻⁶



Obesity is a chronic, multifactorial disease influenced by factors beyond just diet and physical activity¹

1

Mounjaro is the first-and-only treatment activating both the **GIP and GLP-1 receptors** to target the pathophysiology of obesity⁵



Obesity is associated with several complications, **including T2D, hypertension, and PCOS.**² Obesity leads to more than **4 million premature deaths** per year³



People taking Mounjaro 15 mg significantly reduced their body **weight** by an average of **23.6 kg (22.5%)**^{6,*}



The use of **pharmacotherapy in addition to lifestyle changes** may help patients achieve **their weight management goals**⁴



Improvements demonstrated in key cardiometabolic parameters (including blood pressure, waist circumference, triglycerides, HDL cholesterol, and LDL cholesterol)^{6,†}

Mounjaro was studied in adults with obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related complication, excluding type 2 diabetes.^{5,6}

All participants received lifestyle intervention, including a reduced-calorie diet and increased physical activity.⁶

Mounjaro is indicated for chronic weight management and T2DM in adults and is NOT indicated for any cardiometabolic diseases including hypertension, hypertriglyceridemia or dyslipidemia.

Mounjaro is not indicated for the treatment of hyperlipidemia, hypertension and prediabetes.

*Efficacy estimand, MMRM analysis, mITT population (efficacy analysis set). †The efficacy estimand for individual doses was not adjusted for multiplicity, with the exception of waist circumference 10 mg and 15 mg.

1. Bray GA, et al. *Lancet*. 2016;387(10031):1947-1956. 2. Horn DB, et al. *Postgrad Med*. 2022;134(4):359-375. 3. Longo M, et al. *Int J Mol Sci*. 2019;20(9):2358. 4. Apovian CM, et al. *J Clin Endocrinol Metab*. 2015;100(2):342-362. 5. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE. 6. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216 (and supplementary appendix).

Personalized Dosing

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Now Available!

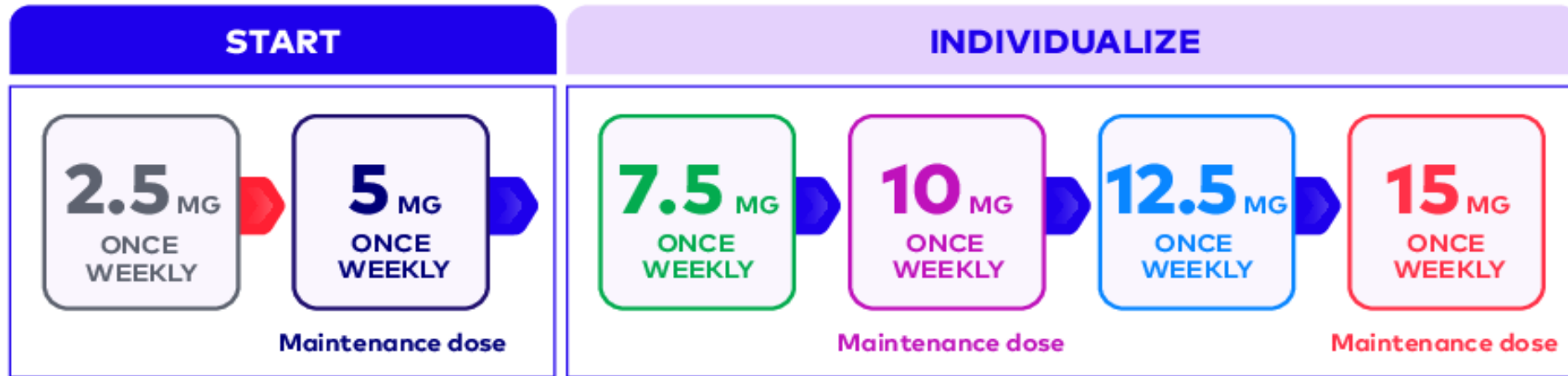
Mounjaro KwikPen is a disposable multi-dose, pre-filled pen with four fixed doses offering four weeks of treatment ¹



1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

Starting and Continuing Mounjaro¹

A Once-Weekly Subcutaneous Injection¹



Start Mounjaro with 2 easy steps

- 1 Initiate with the 2.5-mg starting dose
- 2 After 4 weeks, escalate to the 5-mg dose
If needed, you can continue to increase the dose by 2.5 mg after at least 4 weeks at the current dose

Recommended maintenance doses are 5 mg, 10 mg, and 15 mg (maximum dose)¹

1. Mounjaro (tirzepatide weekly injection) Prescribing Information, UAE.

For adults with T2D and/or obesity (BMI of ≥ 30 kg/m²) or with overweight (BMI of ≥ 27 kg/m²) with at least 1 weight-related comorbidity.

Prescribing Information

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for *Prescribing Information*

