The obesity guidelines and Practical obesity management

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Disclosures

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Definition of Obesity

- Obesity is a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications, and reduces one's lifespan.

Clinical Practice Guideline
for the Management of Obesity in Adults in South Africa

Key concepts

- Obesity can be seen as two distinct, overlapping issues, namely the **personal fat threshold** and the **global rise in body weight**. These two key concepts have often been conflated, but require separate attention.

May W, Goedecke JH, Conradie-Smit M. The science of obesity.
S Afr Med J 2025;115(8b):e3600. https://doi.org/10.7196/SAMJ.2025.v115i8b.3600

Key concepts

- The **first key concept** concerns the **personal fat threshold (PFT).**
- This concept refers to an individual's susceptibility to developing obesity-related conditions, such as type 2 diabetes, once they surpass a certain level of fat accumulation. Essentially, crossing this threshold triggers metabolic complications.

May W, Goedecke JH, Conradie-Smit M. The science of obesity.
S Afr Med J 2025;115(8b):e3600. https://doi.org/10.7196/SAMJ.2025.v115i8b.3600

Key concepts

- The **second key concept** in the obesity landscape is the **global rise in body weight**.
- While this phenomenon is linked to PFTs, it **primarily concerns the factors driving individuals' weight towards and beyond these thresholds**.
- In other words, although each person has **distinct organ-specific fat thresholds**, these thresholds may not be reached without external forces promoting weight gain.
- Notably, these PFTs may be achieved with a normal BMI.
- In addition to driving an individual toward their PFT, **excessive fat mass can also lead to mechanical complications,** either on their own, concurrently with, or in combination with PFT-related problems.

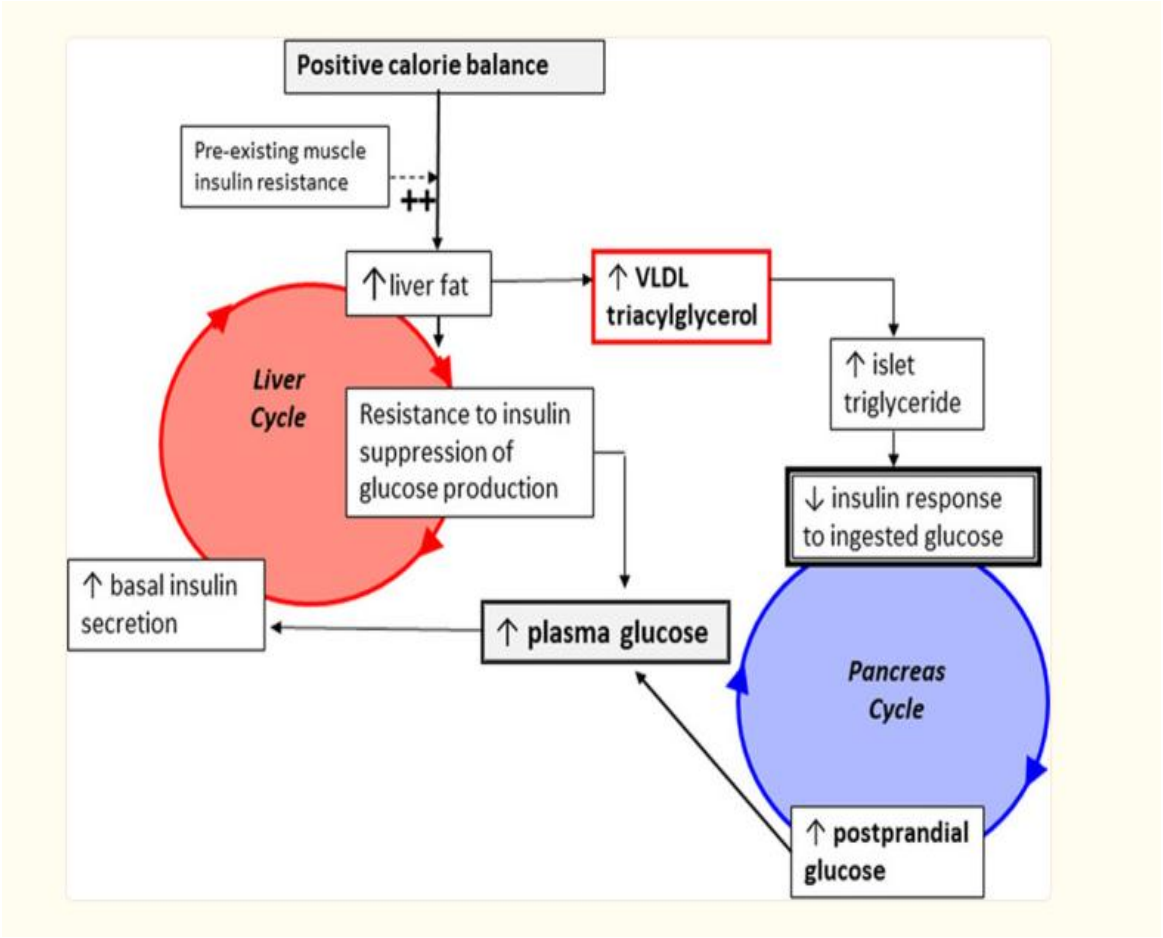
May W, Goedecke JH, Conradie-Smit M. The science of obesity.
S Afr Med J 2025;115(8b):e3600. https://doi.org/10.7196/SAMJ.2025.v115i8b.3600

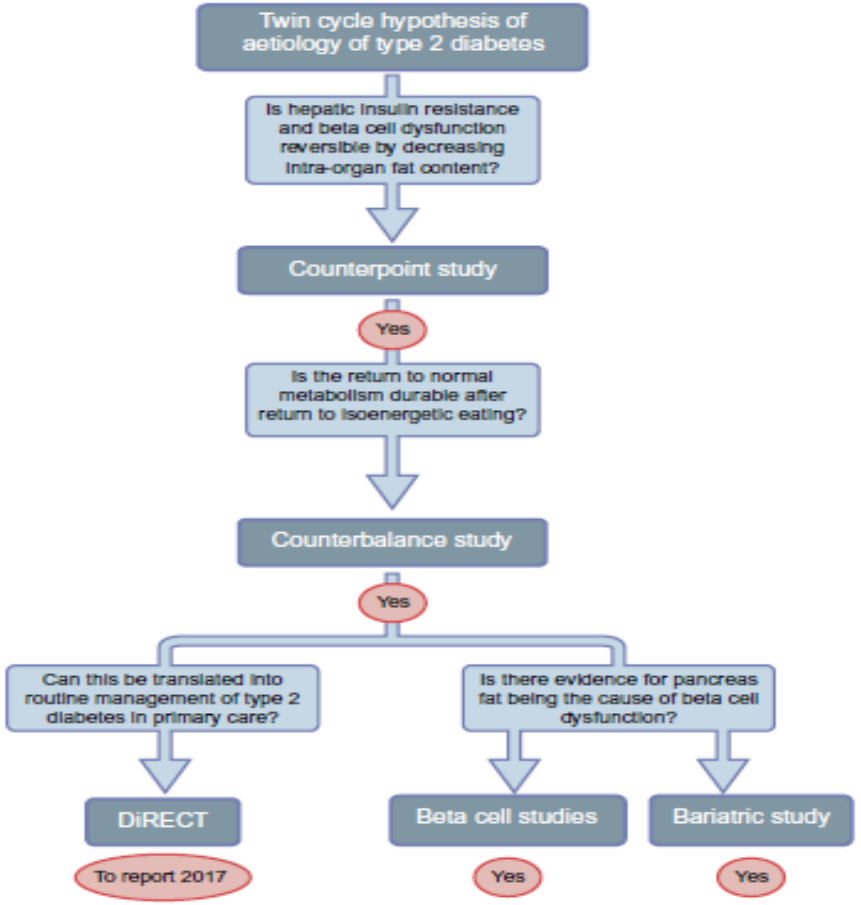
Personal Fat Threshold

Personal Fat Threshold (PFT) is the susceptibility to developing excess adiposity related conditions, and when someone gains sufficient weight to cross their PFT, they will trigger a complication e.g. diabetes

Roy Taylor, Rury R. Holman; Normal weight individuals who develop Type 2 diabetes: the personal fat threshold. *Clin Sci (Lond)* 1 April 2015; 128 (7): 405–410. doi: https://doi.org/10.1042/CS20140553

Twin Cycle Hypothesis





Taylor, R. Pathogenesis of type 2 diabetes: tracing the reverse route from cure to cause. *Diabetologia* **51**, 1781–1789 (2008). https://doi.org/10.1007/s00125-008-1116-7

DiRECT Study

BMI 27-45

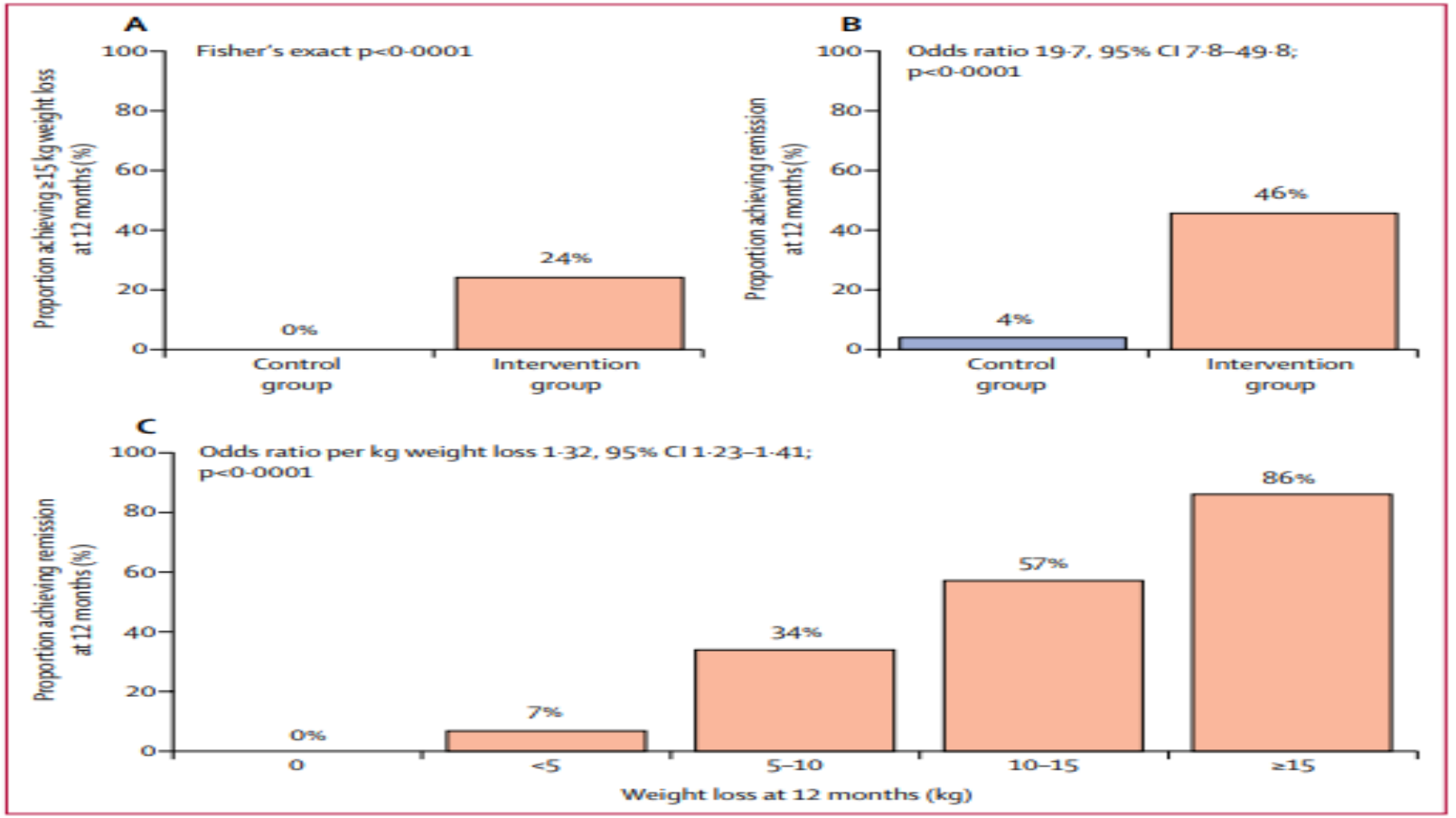
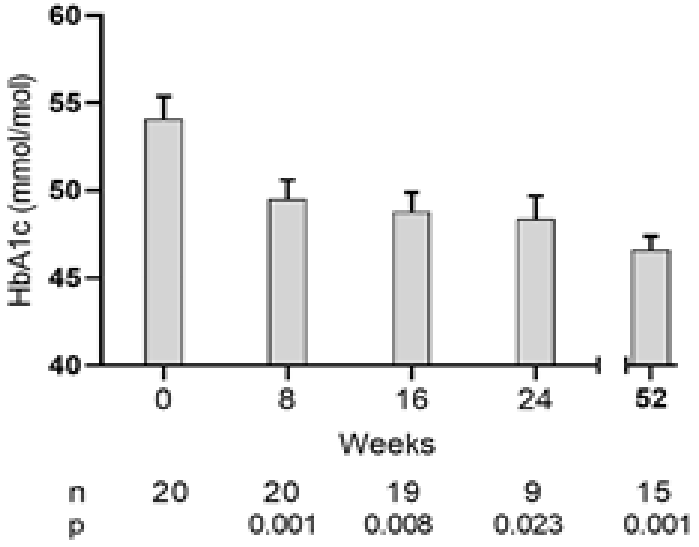


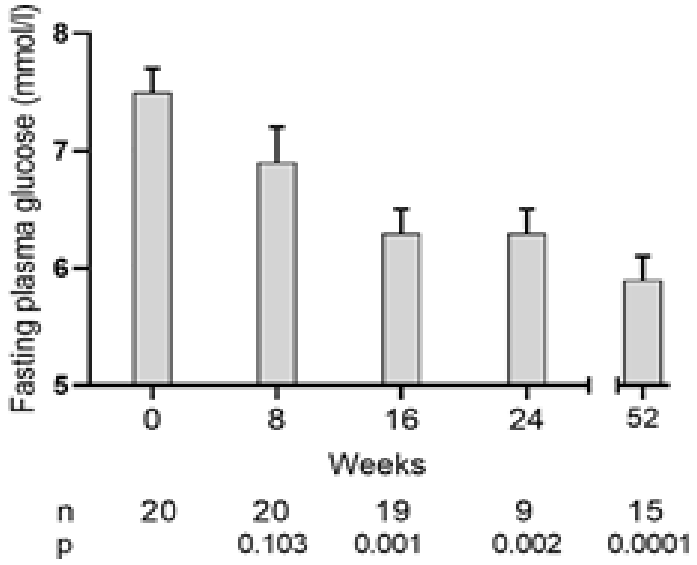
Figure 2: **Primary outcomes and remission of diabetes in relation to weight loss at 12 months**
(A) First co-primary outcome: achievement of at least 15 kg weight loss at 12 months. (B) Second co-primary outcome: remission of diabetes (glycated haemoglobin <6·5% [48mmol/mol], off antidiabetic medication for 2 months). (C) Remission of diabetes, in relation to weight loss achieved at 12 months (both groups combined).

Lean, M. E., Leslie, W. S., Barnes, A. C., Brosnahan, N., Thom, G., McCombie, L., … Taylor, R. (2018). Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. The Lancet, 391(10120), 541–551. doi:10.1016/s0140-6736(17)33102-

ReTUNE STUDY

BMI of 24.8 ± 1.7 (range 21.2–26.9) kg/m2

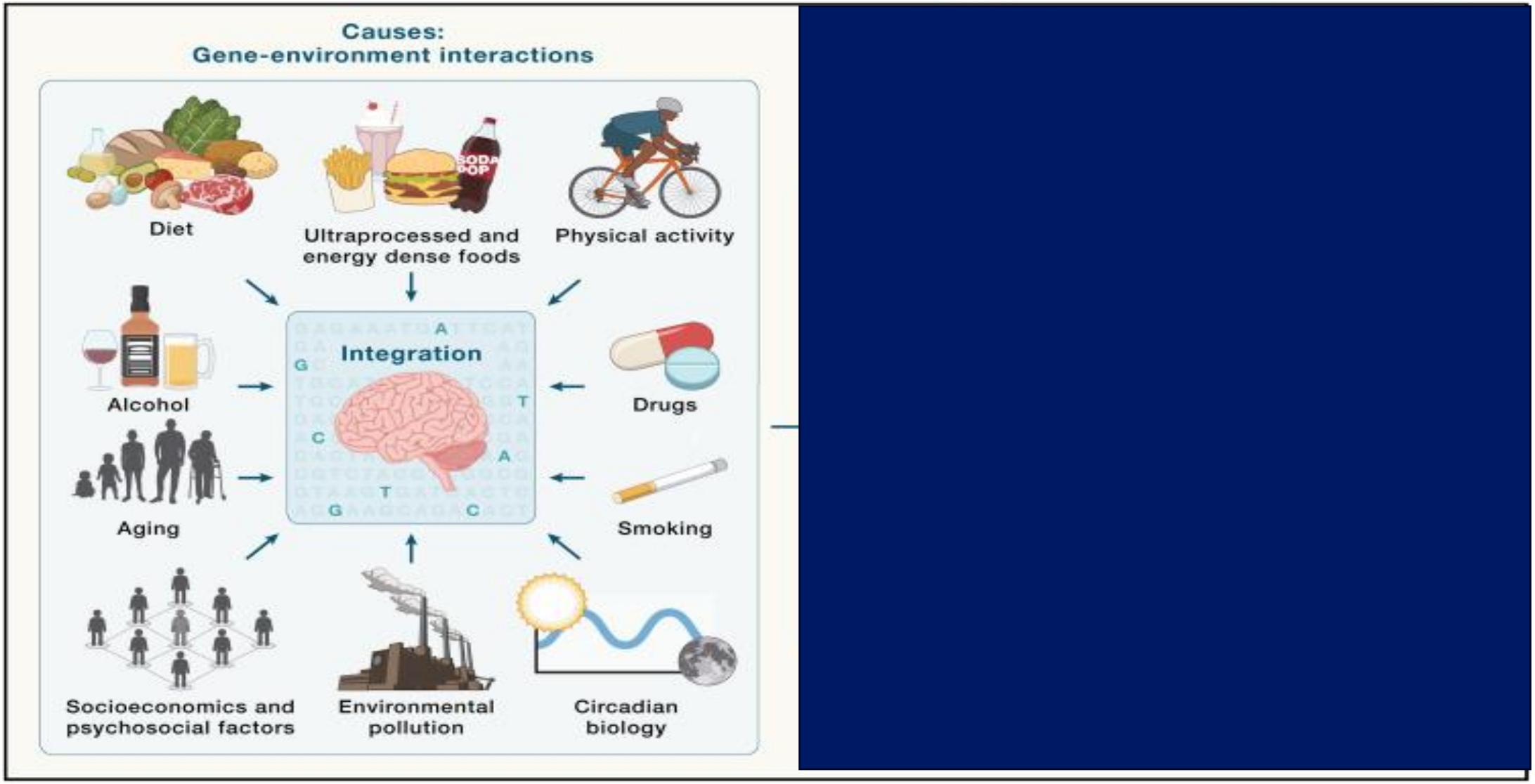




70% reduction in diabetes at 1 year

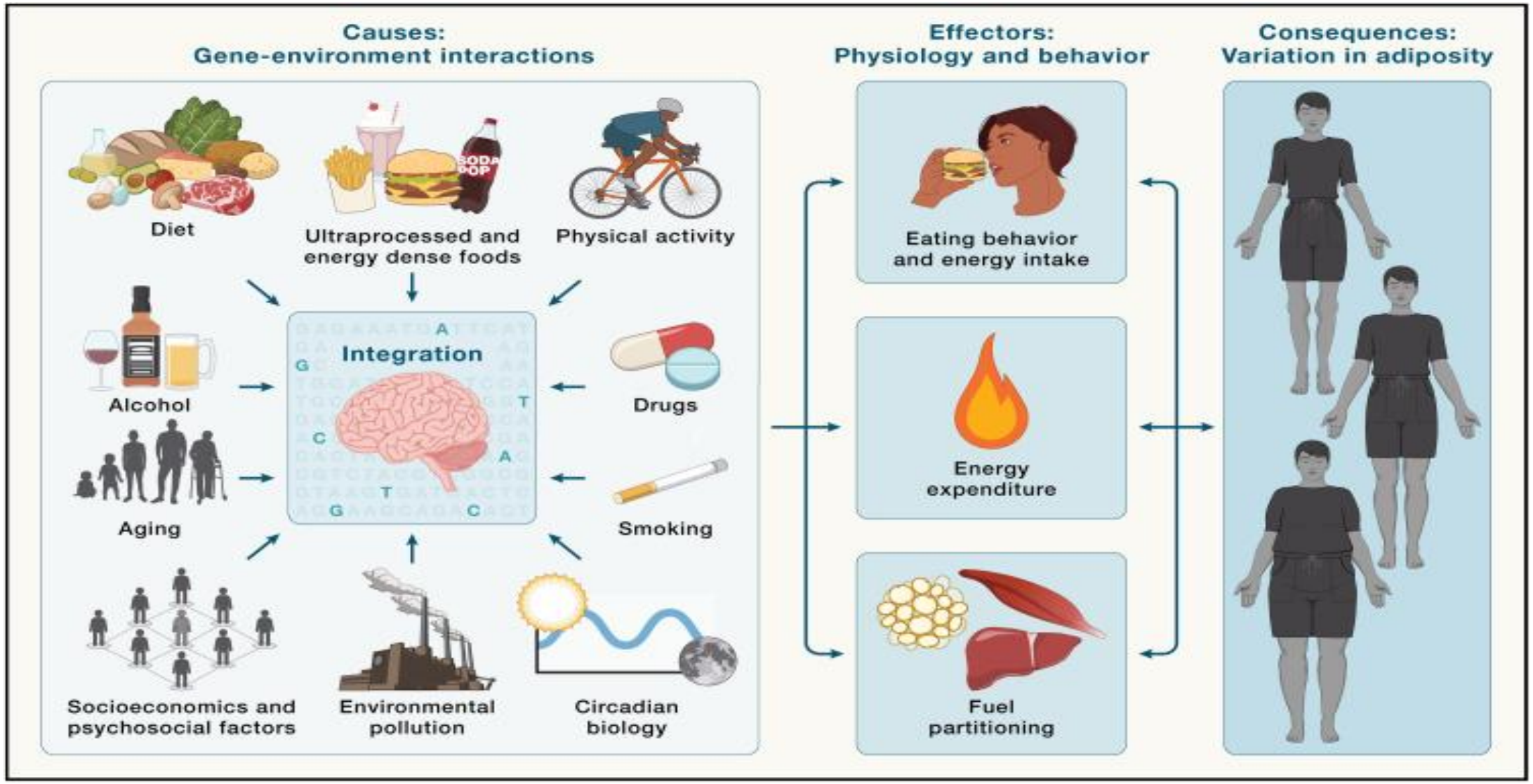
Roy Taylor, Alison C. Barnes, Kieren G. Hollingsworth, Keaton M. Irvine, Alexandra S. Solovyova, Lucy Clark, Tara Kelly, Carmen Martin-Ruiz, Davide Romeres, Albert Koulman, Claire M. Meek, Benjamin Jenkins, Claudio Cobelli, Rury R. Holman; Aetiology of Type 2 diabetes in people with a 'normal' body mass index: testing the personal fat threshold hypothesis. *Clin Sci (Lond)* 31 August 2023; 137 (16): 1333–1346.
doi: https://doi.org/10.1042/CS20230586

Pathophysiology

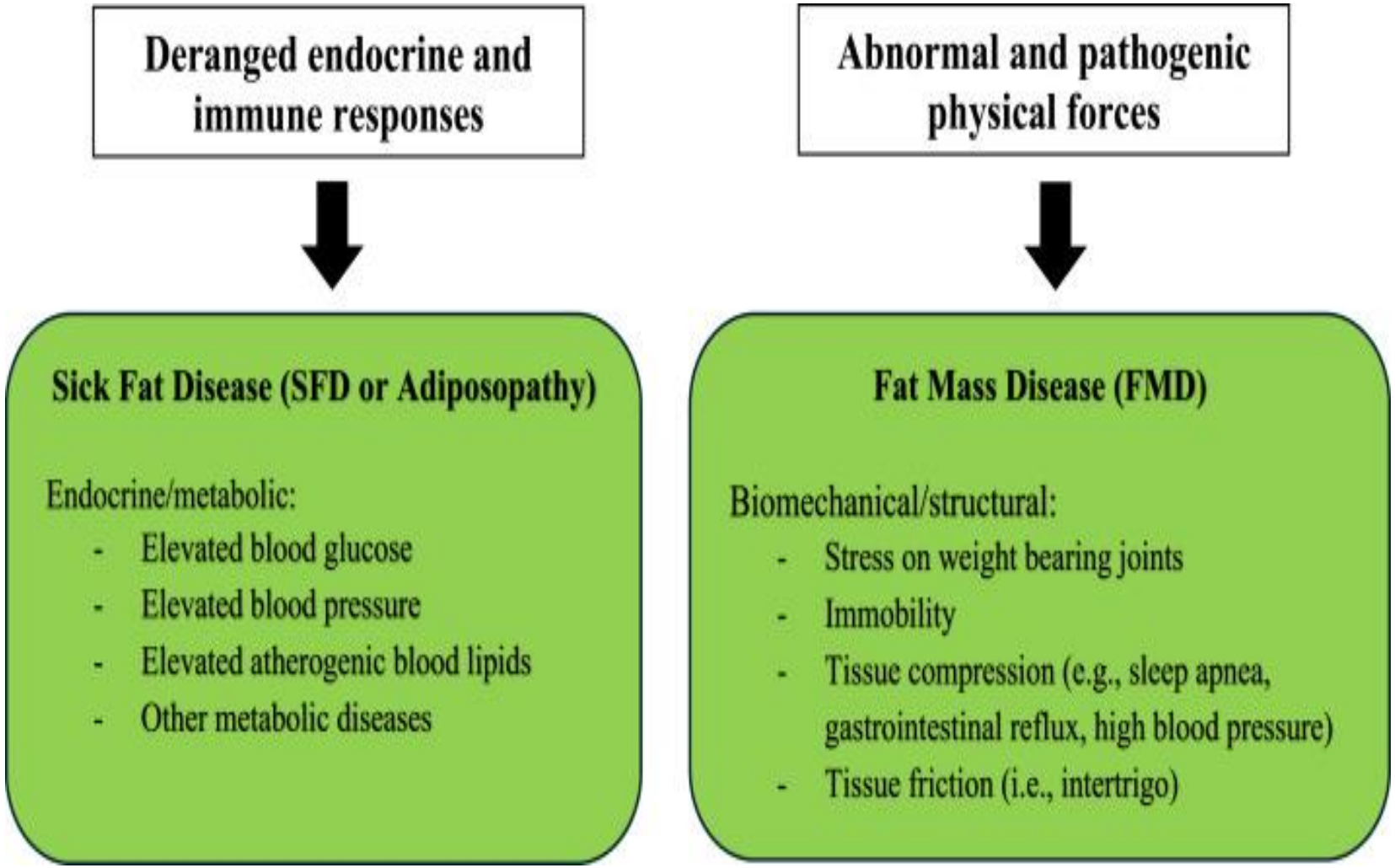


Johansen VB, Petersen J, Lund J, Mathiesen CV, Fenselau H, Clemmensen C. Brain control of energy homeostasis: Implications for anti-obesity pharmacotherapy. Cell. 2025 Aug 7;188(16):4178-212.

Pathophysiology



Johansen VB, Petersen J, Lund J, Mathiesen CV, Fenselau H, Clemmensen C. Brain control of energy homeostasis: Implications for anti-obesity pharmacotherapy. Cell. 2025 Aug 7;188(16):4178-212.



Pennings N, Varney C, Hines S, Riley B, Happel P, Patel S, Bays HE. Obesity management in primary care: A joint clinical perspective and expert review from the Obesity Medicine Association (OMA) and the American College of Osteopathic Family Physicians (ACOFP) - 2025. Obes Pillars. 2025 Mar 17;14:100172. doi: 10.1016/j.obpill.2025.100172. PMID: 40235850; PMCID: PMC11997402.
Obes Facts. 2019;12(2):131-136. doi:10.1159/000497124

Obesity is associated with multiple complications

1. **Metabolic**
2. **Mechanical**
3. **Mental**

- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Infertility
- Incontinence
- Knee osteoarthritis

- GERD
- Cancers*
- Physical functioning

- Sleep apnoea
- Cardiovascular diseases
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - HFpEF
- Chronic back pain
- Type 2 diabetes
  Prediabetes
- Thrombosis
- Gout

*Including breast, colorectal, endometrial, oesophageal, kidney, ovarian, pancreatic and prostate.
GERD, gastro-oesophageal reflux disease; HFpEF, heart failure with preserved ejection fraction; NAFLD, non-alcoholic fatty liver disease.
Adapted from: Sharma. *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.

Classification of obesity

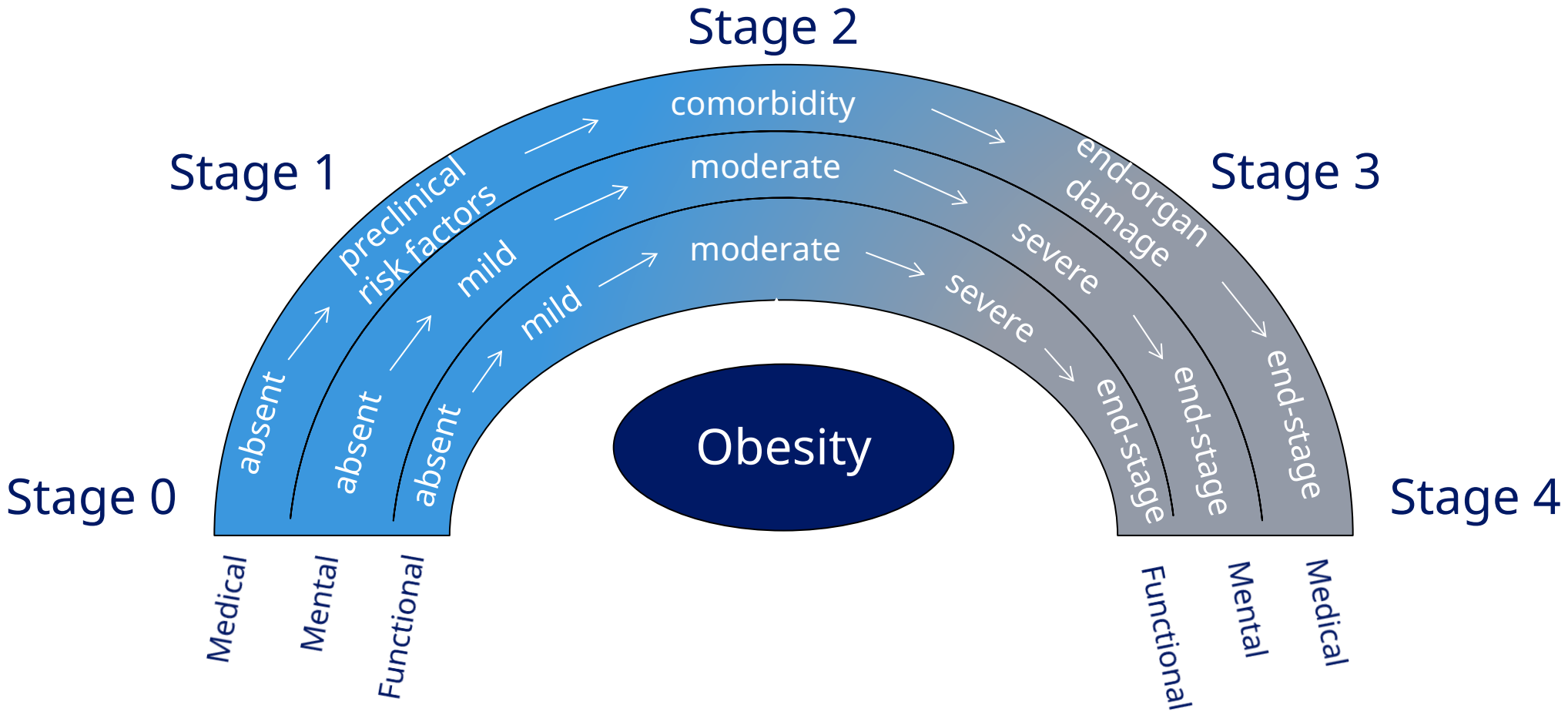
- Obesity is defined as abnormal or excessive fat accumulation that may impair health
- Body mass index (BMI) provides the most convenient population-level measure of overweight and obesity currently available

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

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

**Previously described as overweight according to WHO nomenclature.*
BMI, body mass index; JASSO, Japan Society for the Study of Obesity; WHO, World Health Organization.
1. WHO. Obesity: preventing and managing the global epidemic. 2000. Available from https://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/. Accessed May 2020;
2. Misra A et al. J Assoc Physicians India. 2009;57:163–70; 3. Guidelines for the management of obesity disease 2016 (Japan), issued by JASSO.

Edmonton Obesity Staging System



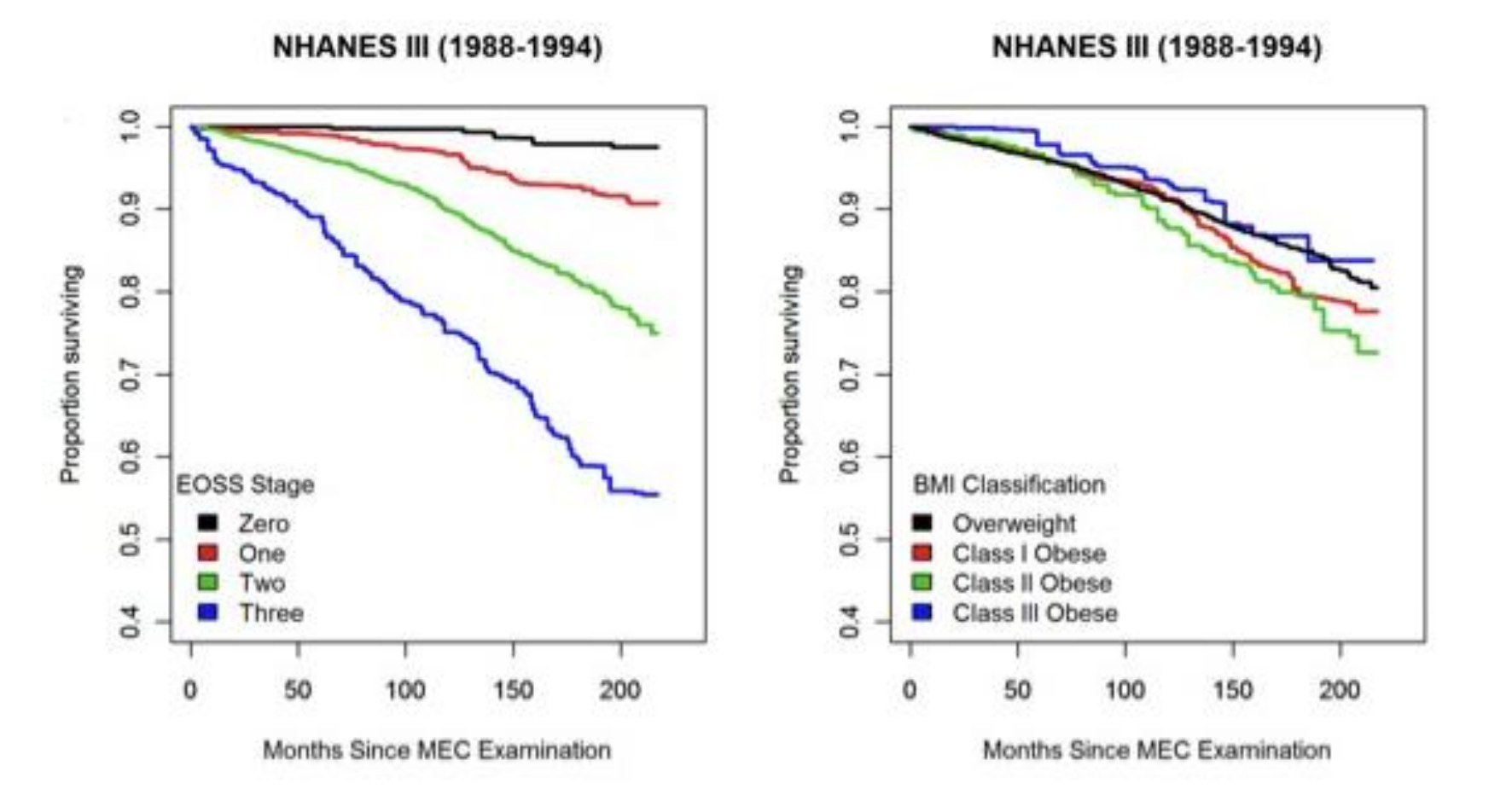
Sharma AM et al. Int J Obes (Lond) 2009; 33(3):289–295; Edmonton Obesity Staging System Chart. Available at: www.drsharma.ca/wp-content/uploads/edmonton-obesity-staging-system-staging-tool.pdf.

STAGE 0	STAGE 1	STAGE 2	STAGE 3	STAGE 4
• **NO** sign of obesity-related risk factors • **NO** physical symptoms • **NO** psychological symptoms • **NO** functional limitations	• Patient has obesity-related **SUBCLINICAL** risk factors *(borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.)* -OR: • **MILD** physical symptoms -patient currently not requiring medical treatment for comorbidities *(dyspnea on moderate exertion, occasional aches/pains, fatigue, etc.)* -OR: • **MILD** obesity-related psychological symptoms and/or mild impairment of well-being *(quality of life not impacted)*	• Patient has **ESTABLISHED** obesity-related comorbidities requiring medical intervention *(HTN, Type 2 Diabetes, sleep apnea, PCOS, osteoarthritis, reflux disease)* -OR: • **MODERATE** obesity-related psychological symptoms *(depression, eating disorders, anxiety disorder)* -OR: • **MODERATE** functional limitations in daily activities *(quality of life is beginning to be impacted)*	• Patient has **SIGNIFICANT** obesity-related end-organ damage *(myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis)* -OR: • **SIGNIFICANT** obesity-related psychological symptoms *(major depression, suicide ideation)* -OR: • **SIGNIFICANT** functional limitations *(e.g., unable to work or complete routine activities, reduced mobility)* • **SIGNIFICANT** impairment of well-being *(quality of life is significantly impacted)*	• **SEVERE** *(potential end stage)* disabilities from obesity-related comorbidities -OR: • **SEVERELY** disabling psychological symptoms -OR: • **SEVERE** functional limitations

Source: Sharma, A. M. & Kushner, R. F. (2009). A proposed clinical staging system for obesity. International Journal of Obesity (2005), 33 (3), 289–295. https://www.ottawahospital.on.ca/fr/documents/2017/05/edmonton-obesity-staging-system-staging-tool.pdf

ASSESS

EOSS Predicts Mortality in NHANES III



Padwal R, Sharma AM et al. CMAJ 2011

Obesity Redefined

Then…

"Obesity is defined by a BMI of ≥ 30 kg/m^2

Now…

"Obesity is a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications and reduces lifespan"

.

Brown et al. Canadian Adult Obesity Clinical Practice Guidelines: Medical Nutrition Therapy in Obesity Management. Available from: https://obesitycanada.ca/guidelines/nutrition. Accessed August 10, 2020.

Moving Beyond BMI

Clinical trials use BMI to define obesity. Limitations include:

- BMI does not provide info on body composition or fat distribution
- It is not a direct measure of fat
- Non-ethnicity specific BMI criteria were used

Other anthropometric measures correlate strongly with adiposity-related complications:

Bedside

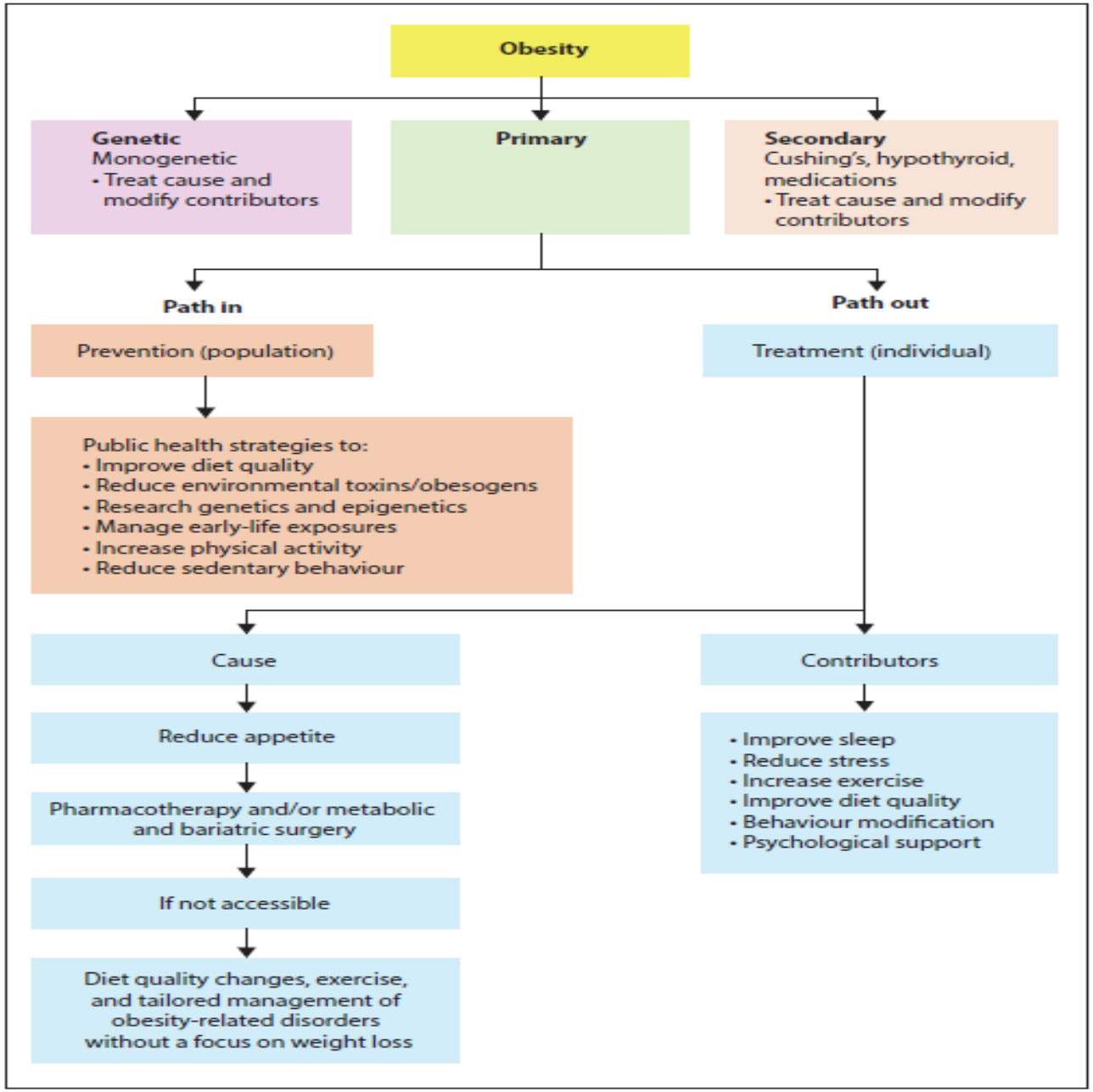
- Waist circumference
- Waist-to-hip ratio
- Waist-to-height ratio (0.5)

Non-bedside

- Dexa
- BIA
- CT
- MRI

Murphy A, Diab PN, Goedecke JH, Conradie-Smit M, May W. Assessment of people living with obesity. *S Afr Med J* 2025;115(9b):e3730. https://doi.org/10.7196/SAMJ.2025.v115i9b.3730

Clinical Practice Guidelines for the Management of Obesity in Adults in South Africa



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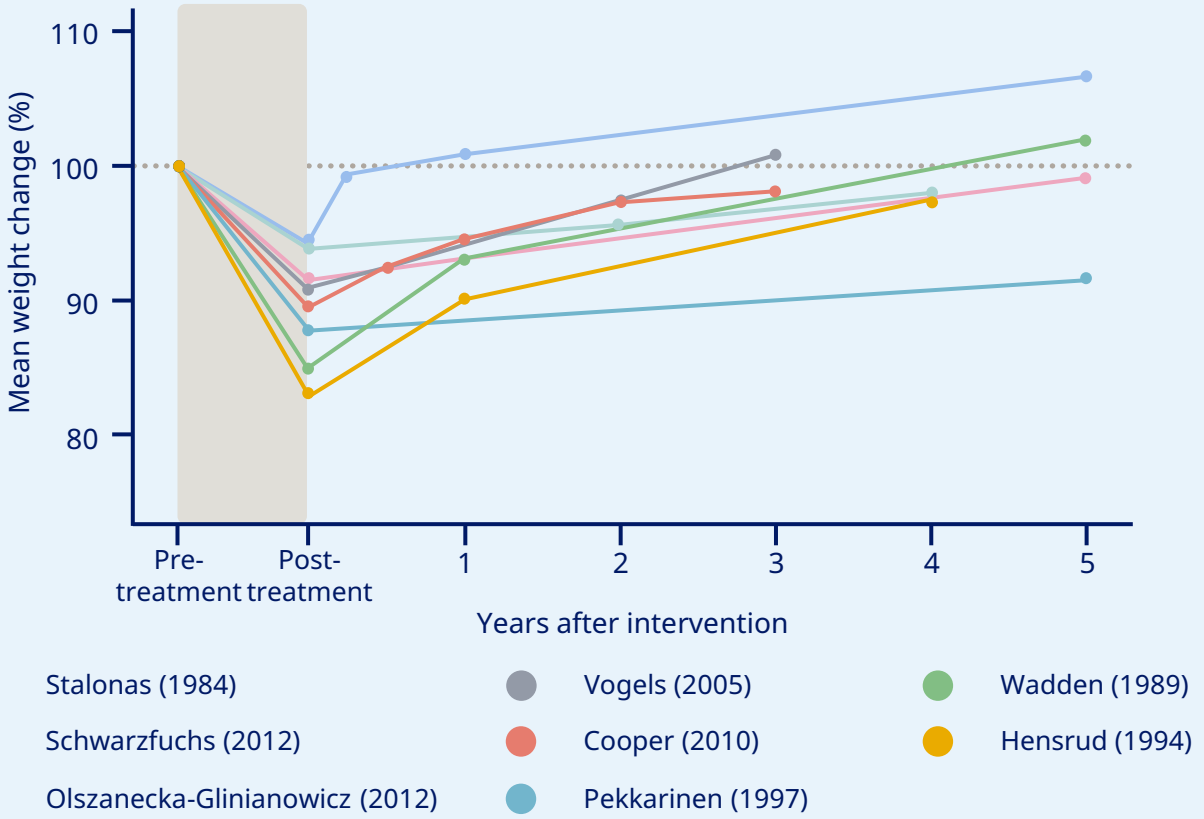
How successful are lifestyle interventions in chronic weight management?

Maintenance of weight loss[1]:



Weight loss following lifestyle interventions is not sustainable in the long-term

Most individuals regain more than half of the weight lost within 2 years and more than 80% within 5 years[2].

Moreover, lifestyle interventions often result in modest weight loss (3–5%).

Diet & exercise alone <5% weight loss[2]

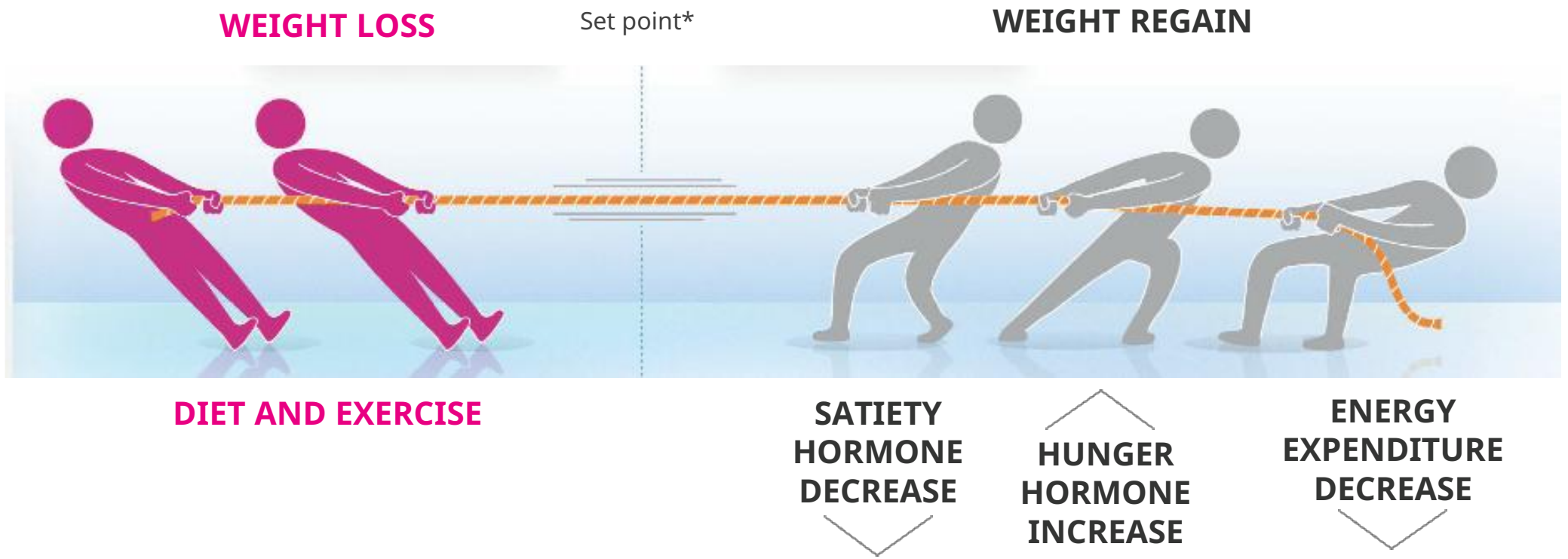
Sustained weight loss leads to health benefits and improvements in quality of life[3]

Maintenance of weight loss

1. Nordmo M et al. Obes Rev. 2020;21:e12949; ; 2. Horn D et al. Postgrad Med. 2022;134:359–75.

Maintaining weight loss and associated health benefits is hard because biology drives weight regain[1-3]

Despite your patients' best efforts, hormonal changes after weight loss can prevent them from keeping the weight off[1-3]



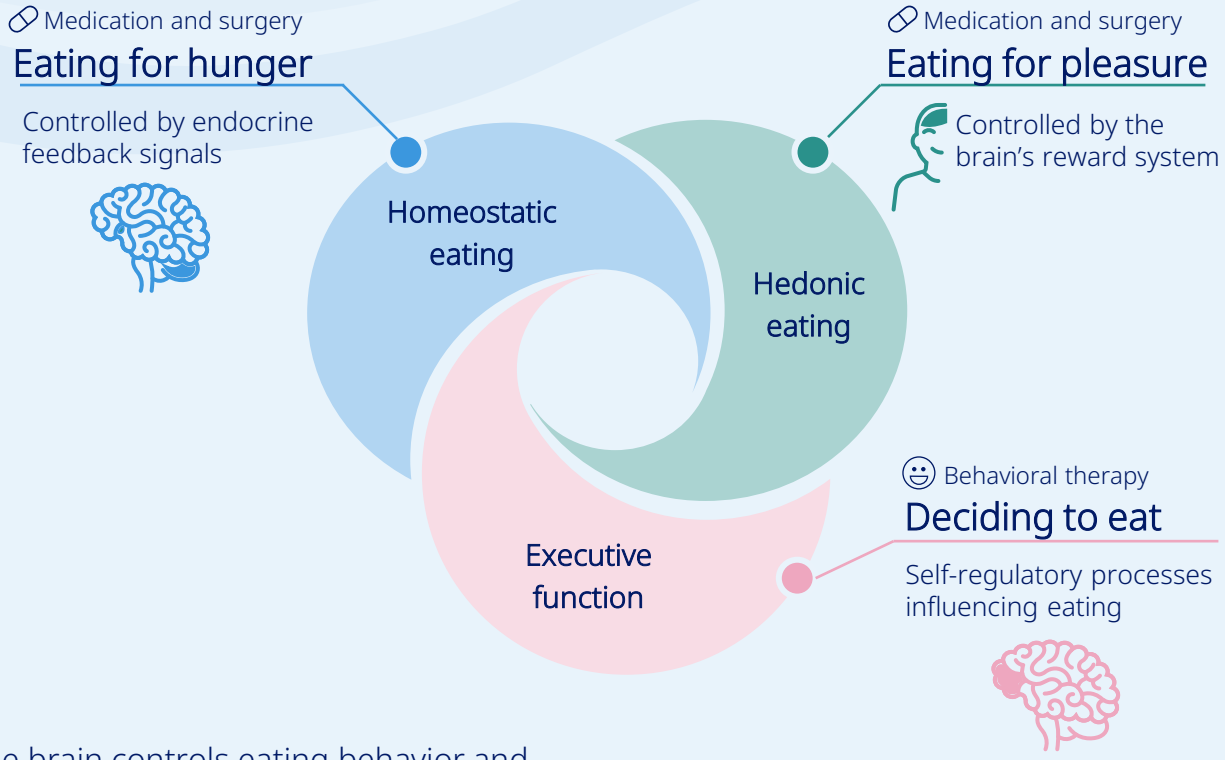
Sustained weight loss is associated with ongoing improvements across a range of complications[4]

Weight regain puts people at risk of developing or worsening some obesity-related complications[5]

*Set point is a theory that suggests the body has a predetermined weight range, or "set point", that it defends against and strives to maintain.[1]

1. Garvey WT. Is obesity or adiposity-based chronic disease curable: the set point theory, the environment, and second-generation medications. Endocr Pract. 2022;28(2):214-222. 2. Sumithran P, Sumitharn P, Prendergast LA, Delbridge E, et al. Long-term persistence of hormonal adaptations to weight loss. N Engl J Med 2011;365(17):1597-1604. 3. Lam YY, Ravussin E. Analysis of energy metabolism in humans: a review of methodologies. Mol Metab 2016;5(11):1057-1071. 4. Haase CL, Lopes S, Olsen AH, et al. Weight loss and risk reduction of obesity-related outcomes in 0.5 million people: evidence from a UK primary care database. Int J Obes (Lond). 2021;45(6):1249-1258. 5. King WC, Hinerman AS, Belle SH, et al. Comparison of the performance of common measures of weight regain after bariatric surgery for association with clinical outcomes. JAMA. 2018;320(15):1560-1569.

What is the role of the brain in regulating appetite?



The brain controls eating behavior and appetite. Weight is determined and regulated by a unique, three-layer appetite system.

Appetite is normally regulated by a complex interplay of different signals and areas in the brain

Increased understanding of the biology of appetite regulation has led to the development of new generation pharmacotherapy.

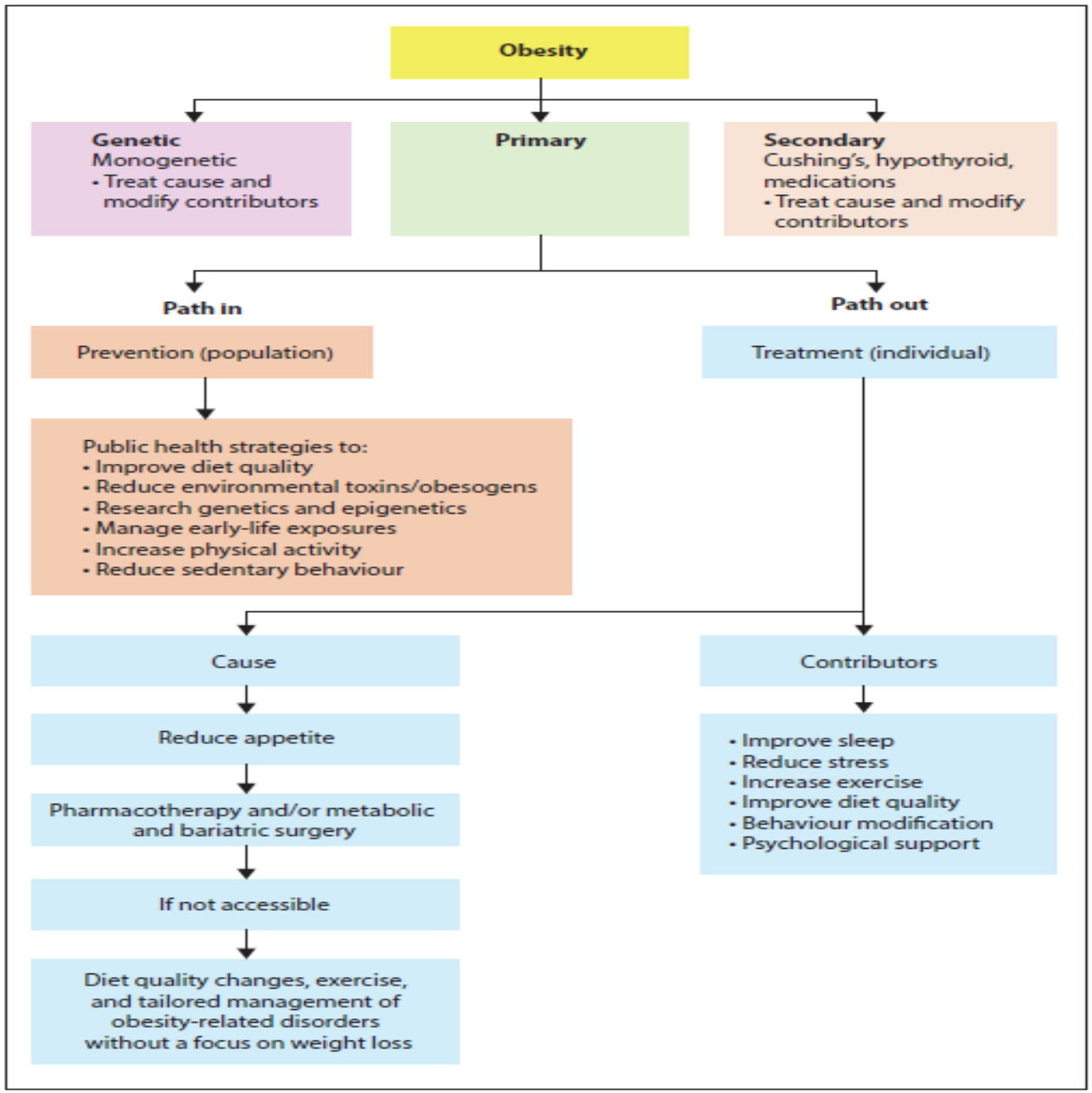
Many paths lead to obesity

Obesity is not simply due to an individual's choice or lack of willpower[7]

Appetite is normally regulated by a complex interplay between gut and brain

1. Badman MK & Flier JS. Science. 2005;307:1909–14; 2. van Bloemendaal L et al. Diabetes. 2014;63:4186–96; 3. Klok MD et al. Obes Rev. 2007;8:21–34; 4. Hall K et al. Am J Public Health. 2014;104:1169–75; 5. Berridge KC et al. Brain Res. 2010;1350:43–64; 6. Vallis M. Clin Obes. 2019;9:e12299; 7. Lau D et al. Canadian Adult Obesity Clinical Practice Guidelines: The Science of Obesity. Available from https://obesitycanada.ca/guidelines/science.

Clinical Practice Guidelines for the Management of Obesity in Adults in South Africa



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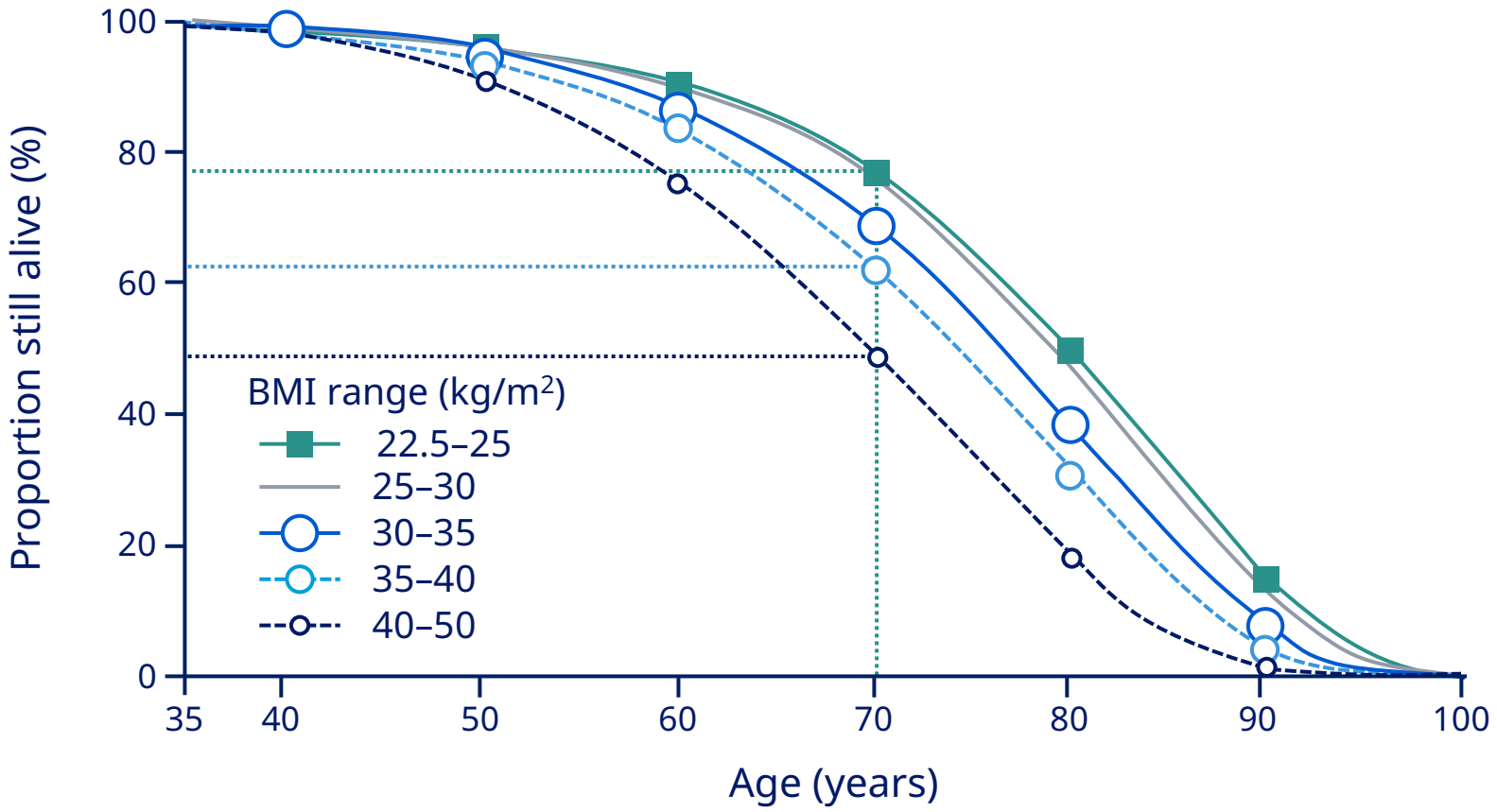
Life expectancy decreases as BMI increases



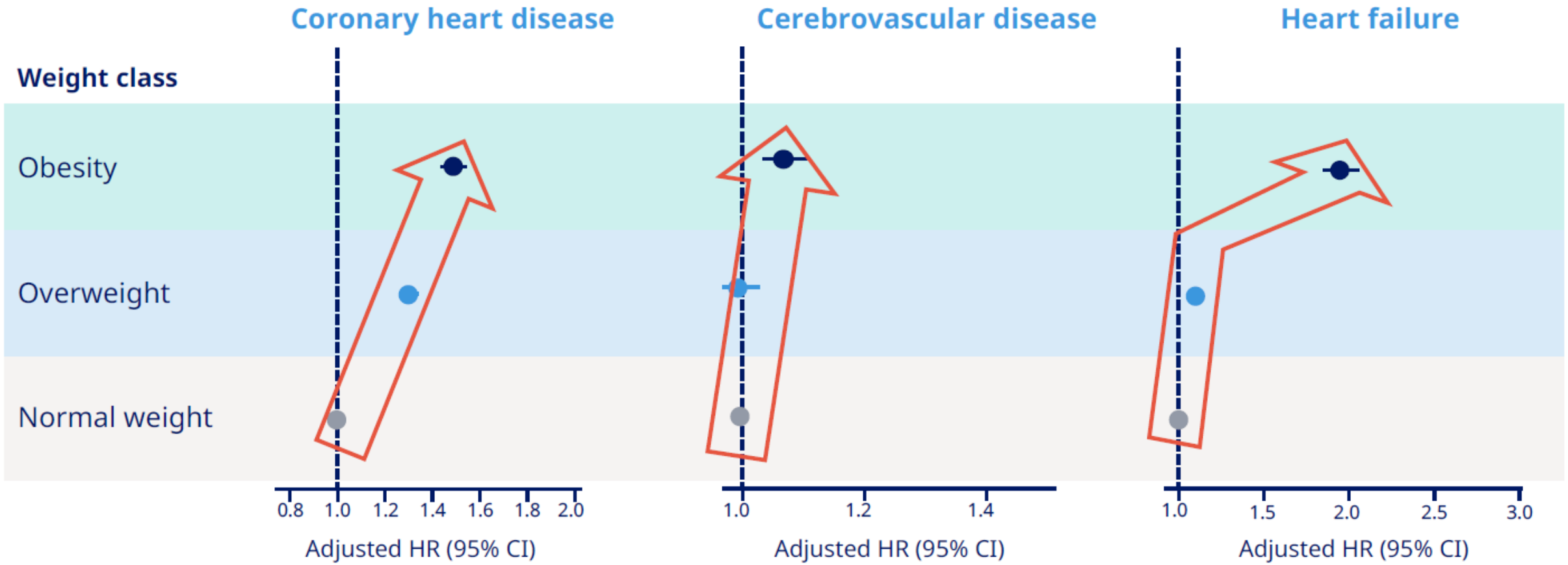
Normal BMI =
almost 80% chance of reaching age 70

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

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

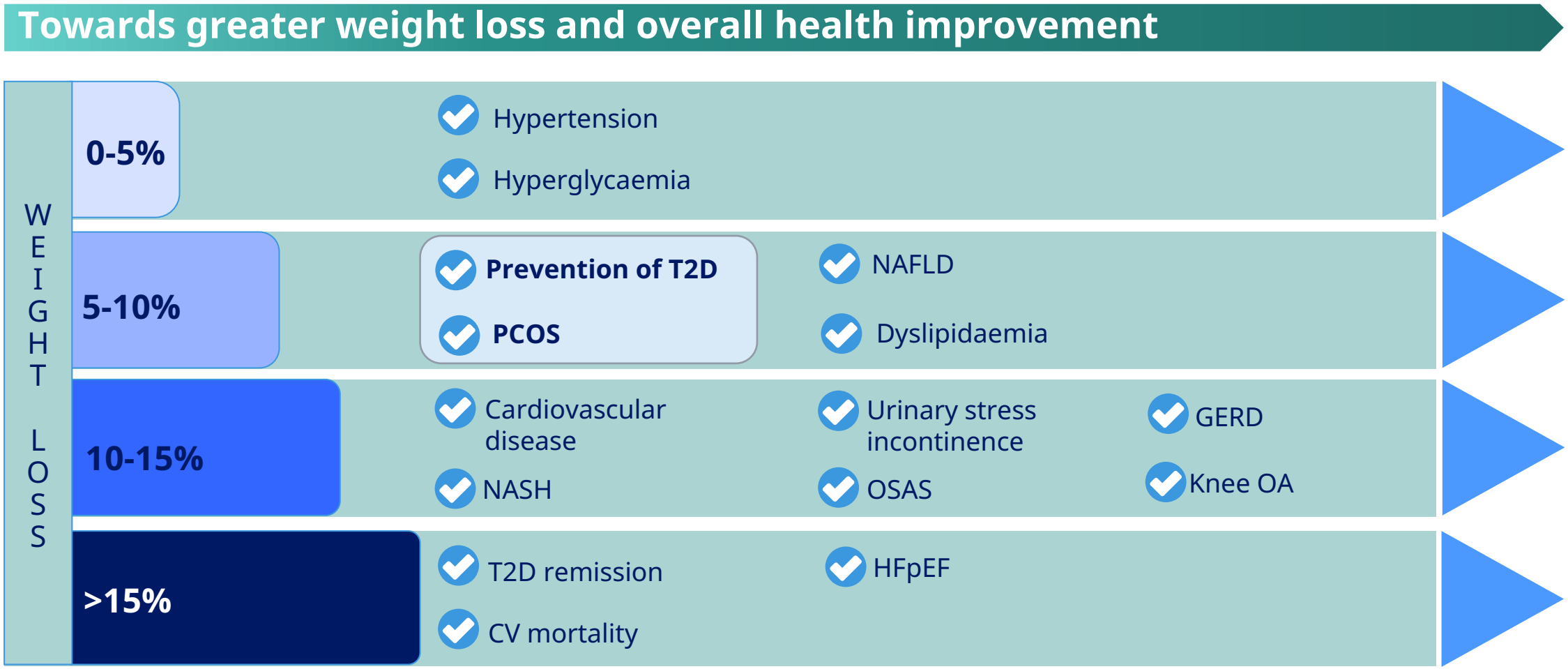
Data are based on male subjects; n=541,452.
BMI, body mass index.
Prospective Studies Collaboration. Lancet. 2009;373:1083–96.

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.
Caleyachetty *et al. J Am Coll Cardiol* 2017;70:1429–37.

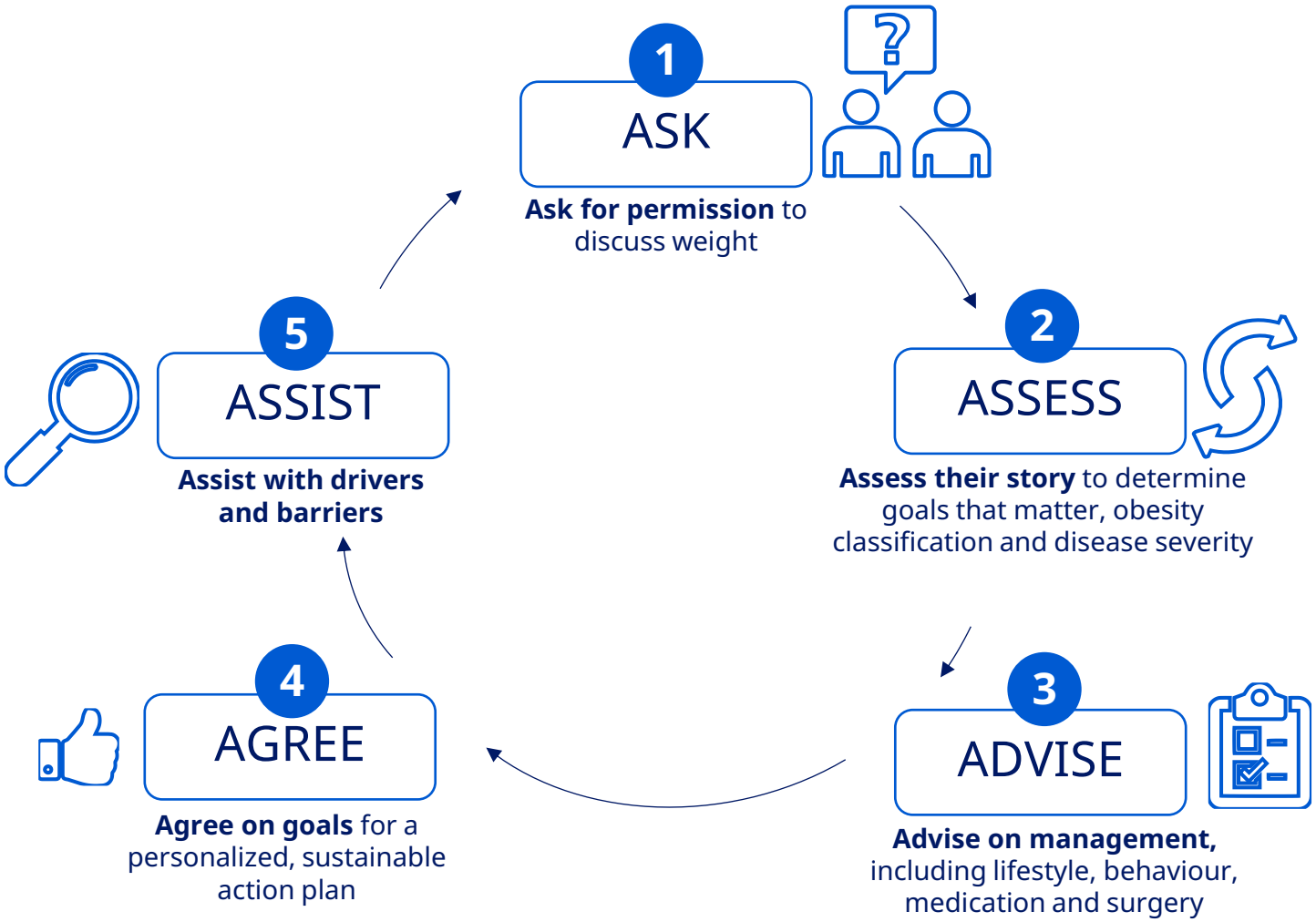
Weight loss and its therapeutic benefits



CV, cardiovascular; GERD, gastro-oesophageal reflux disease; HFpEF, heart failure with preserved ejection fraction; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; OA, osteoarthritis; OSAS, obstructive sleep apnoea syndrome; PCOS, polycystic ovary syndrome; TG, triglycerides.

Adapted from: AACE/ACE Obesity CPG, Endocr Pract. 2016; 22(Suppl 3); Cefalu et al. Diabetes Care 2015; 38(8):1567–1582; Lean et al. Lancet 2018; 391(10120):541–551; Hannah et al. Clin Liver Dis 2016; 20(2):339–350.

5As of obesity management



Wharton S et al. CMAJ 2020; 92(31):E875–E891.

Exercise

- Good for living longer
- Feeling good
- Weight maintenance
- weight loss….need to do a lot

Balance
Posture
Strength

- To **prevent weight gain** of > 3% → **150-250 minutes/week**
- For **weight loss** → **225–420 minutes/week** will result in **5-7.5 kg**.
  A dose-response relationship exists.
- For **weight maintenance** after weight loss → 2**00-300 minutes of exercise/week**
- **Potential problems of increasing exercise….<u>increased appetite</u>**

Donnelly, Joseph E. et al. “American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults.” *Medicine and science in sports and exercise* 41 2 (2009): 459-71 .
Sumithran, P. et al (2011). Long-term persistence of hormonal adaptations to weight loss. The New England journal of medicine, 365(17), 1597–1604. Martin, C. K., Johnson, W. D. et al (2019). Effect of different doses of supervised exercise on food intake, metabolism, and non-exercise physical activity: The E-MECHANIC randomized controlled trial. *The American journal of clinical nutrition*, *110*(3), 583–592.

Nutritional Therapy

- Quality (protein, carbs, fats)
- Quantity (most important)
- Timing (intermittent fasting)

Wei X, Cooper A, Lee I, et al. Intermittent Energy Restriction for Weight Loss: A Systematic Review of Cardiometabolic, Inflammatory and Appetite Outcomes. *Biological Research For Nursing*. 2022;24(3):410-428.
Ge, L., Sadeghirad, et al (2020). Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials. *BMJ (Clinical research ed.)*, *369*, m696

Behavioral Therapy

- **Cognitive Therapy(CBT)** – This type of therapy challenges thoughts, which leads to better behavior and mood.
- **Behavioral Therapy** – This type of therapy uses behavioral approaches to change or alter behaviors for improved outcomes.

Wei X, Cooper A, Lee I, et al. Intermittent Energy Restriction for Weight Loss: A Systematic Review of Cardiometabolic, Inflammatory and Appetite Outcomes. *Biological Research For Nursing*. 2022;24(3):410-428.
Ge, L., Sadeghirad, et al (2020). Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials. *BMJ (Clinical research ed.)*, *369*, m696

Pharmacotherapy registered in South Africa

Pharmacotherapy for obesity management should be offered to individuals with BMI ≥ 30 kg/m^2 * or BMI ≥ 27 kg/m^2 * with adiposity related complications, in conjunction with health behaviour changes:

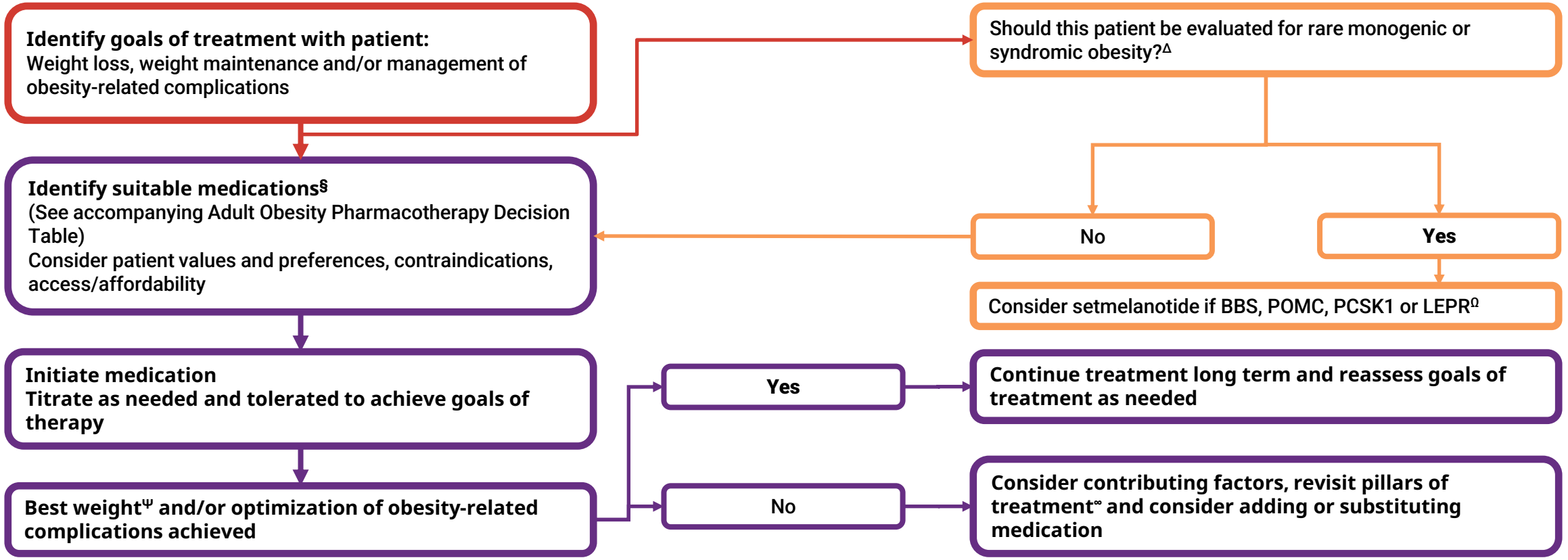
- Semaglutide 2.4 mg weekly (BMI ≥ 27 kg/m^2)
- Tirezpatide 15mg weekly (BMI ≥ 27 kg/m^2)
- Liraglutide 3 mg daily (BMI ≥ 27 kg/m^2)
- Naltrexone/bupropion 16 mg/180 mg BID (BMI 27-45 kg/m^2)
- Orlistat 120 mg TID (BMI 28-47 kg/m^2)

SAHPRA - South African Health Products Regulatory Authority

obesity canada / obésité canada

Canadian Adult Obesity Clinical Practice Guideline

Adult Obesity Pharmacotherapy Decision Tool



Δ Consider genetic testing if early onset obesity with hyperphagia, features of monogenic obesity (see text)

Ω BBS - Bardet-Biedl Syndrome ; POMC - pro-opiomelanocortin deficiency; PCSK1 - proprotein convertase subtilisin/kexin type 1 deficiency; LEPR - leptin receptor deficiency

§ Medications approved in Canada: Liraglutide 3 mg daily, Naltrexone/Bupropion 16/180 mg bid, Orlistat 120 mg tid, Semaglutide 2.4 mg weekly , tirzepatide 5/10/15 mg weekly. All are recommended in conjunction with health behavior changes.

Ψ The weight that a person can achieve and maintain while living their healthiest and happiest life

∞ see https://obesitycanada.ca/wp-content/uploads/2020/10/191707-guide-2-at.pdf

obesity canada / obésité canada

Canadian Adult Obesity Clinical Practice Guideline

Adult Obesity Pharmacotherapy Decision Table

		Liraglutide 3 mg daily	Naltrexone/ Bupropion 16/180 mg BID	Orlistat 120 mg TID	Semaglutide 2.4 mg weekly	Tirzepatide 5/10/15 mg weekly
Cardio-Metabolic Complications	Prediabetes	✓		✓	✓	✓
	T2D	✓	✓	✓	✓	✓ **
	MASH	✓		∅	✓	✓
	ASCVD		🔍		✓	🔍
	HFpEF				✓	✓ *
Mechanical Complications	OSA	✓				✓ **
	OA	∅			✓	🔍
Patient Reported Outcome Measures (PROMS)	QoL	+	+		+	+
	Physical Function	+	+		+	+
	Cravings		+		+	
Average weight loss (placebo subtracted)		5.4%	4.8%	2.9%	12.4%	11.9/16.4/17.8%

✓ Level 1a Very High Certainty

✓ Level 2a Moderate Certainty

✓ Level 3 Low Certainty

∅ No Benefit

\+ Benefit

🔍 In study as identified on www.clinicaltrials.gov

*15 mg, **10 mg or 15 mg . T2D - type 2 diabetes, MASH - metabolic dysfunction-associated steatohepatitis; ASCVD - atherosclerotic cardiovascular disease; HFpEF - heart failure with preserved ejection fraction; OSA - obstructive sleep apnoea; OA - osteoarthritis; QoL - quality of life

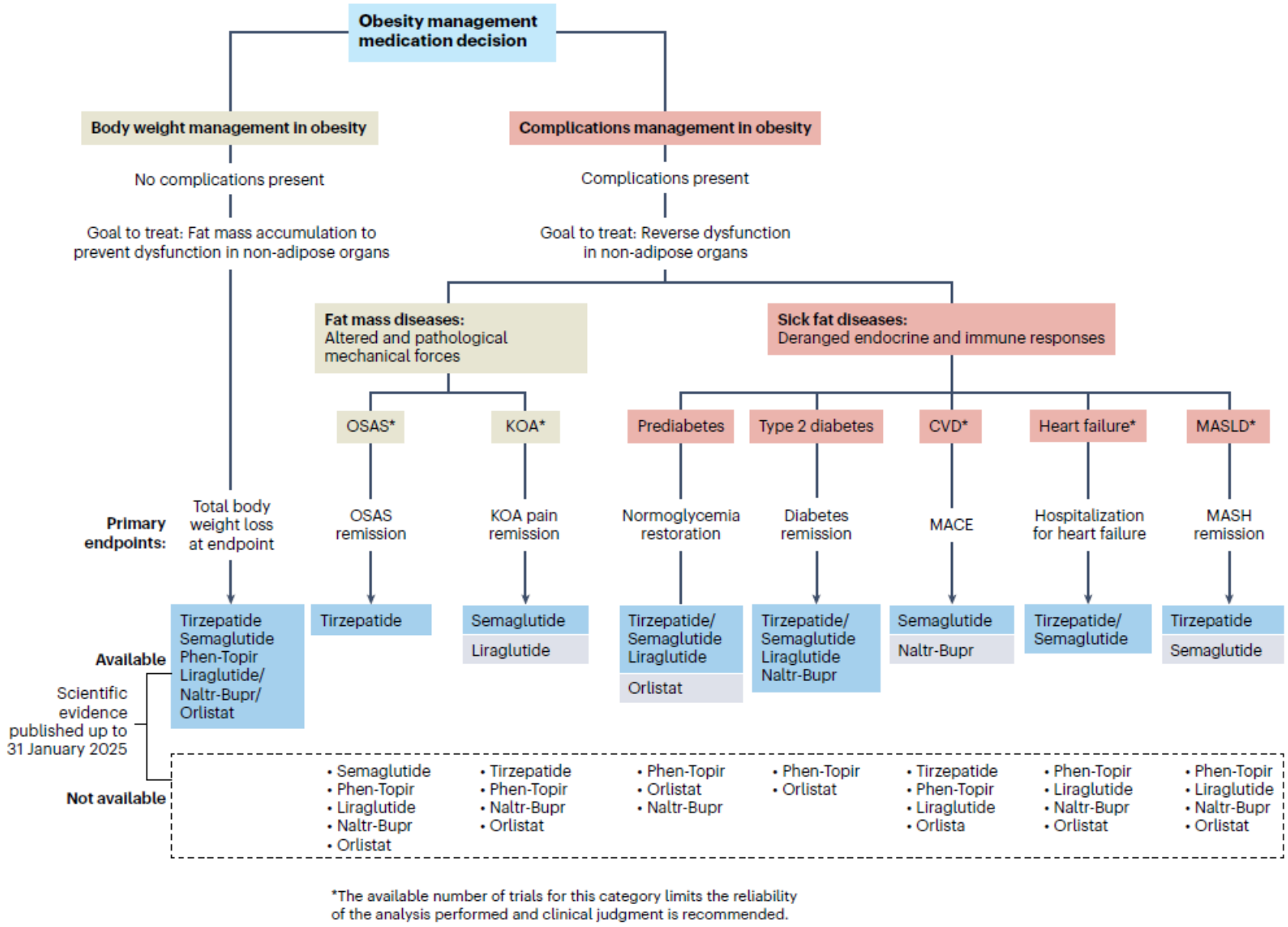
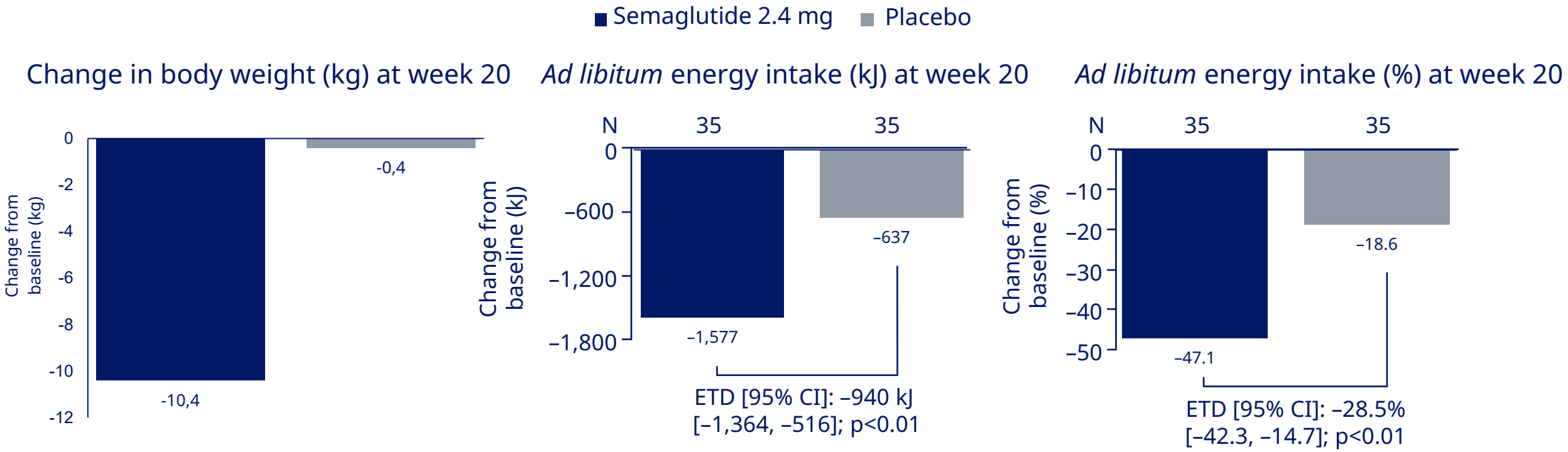


Fig. 1 | Treatment algorithm from the EASO for individuals with obesity. The treatment algorithm is based on the presence or absence of relevant obesity-related medical conditions. The algorithm is grounded in scientific evidence available up to 31 January 2025. Obesity management medications are listed in order of efficacy. Medications with equivalent or comparable efficacy are listed in the same position. Asterisks indicate that the available number of trials for this category limits the reliability of the analysis performed and clinical judgment is recommended. Color coding reflects statistical significance: blue shading indicates statistically significant effects; gray shading denotes obesity medications tested without significant effects. CVD, cardiovascular disease; KOA, knee osteoarthritis; Naltr-Bupr, naltrexone–bupropion; Phen-Topir, phentermine–topiramate.

Semaglutide 2.4 s.c. mg reduces energy intake



BW decreased by **10.4 kg** with semaglutide 2.4 mg compared to 0.4 kg with placebo

Energy intake was **35% lower** with semaglutide 2.4 mg compared to placebo

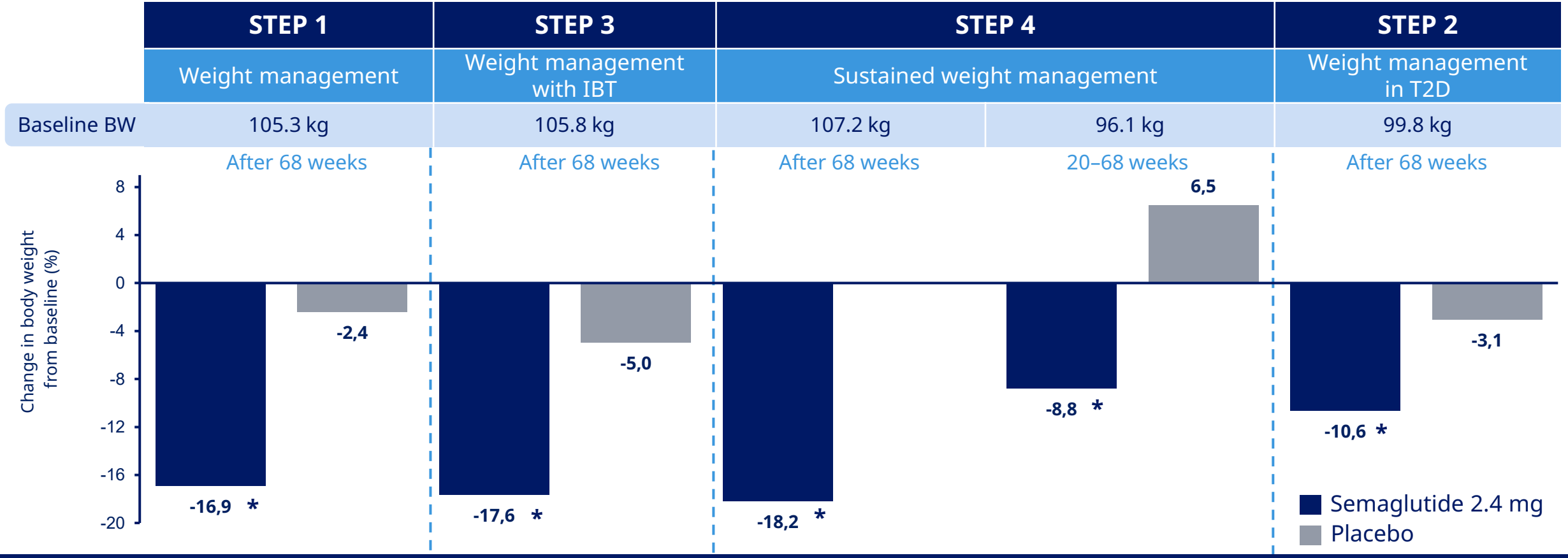
Energy intake was **47% lower** with semaglutide 2.4 mg compared to baseline

BW, body weight; CI, confidence interval; ETD, estimated treatment difference. S.c. subcutaneous

Skovgaard D et al. Presented at the 56th European Association for the Study of Diabetes (EASD) virtual meeting, 22–25 September 2020. Poster Number: 555.

Weight loss across STEP 1–4

Effects of semaglutide 2.4 mg once-weekly in patients with obesity



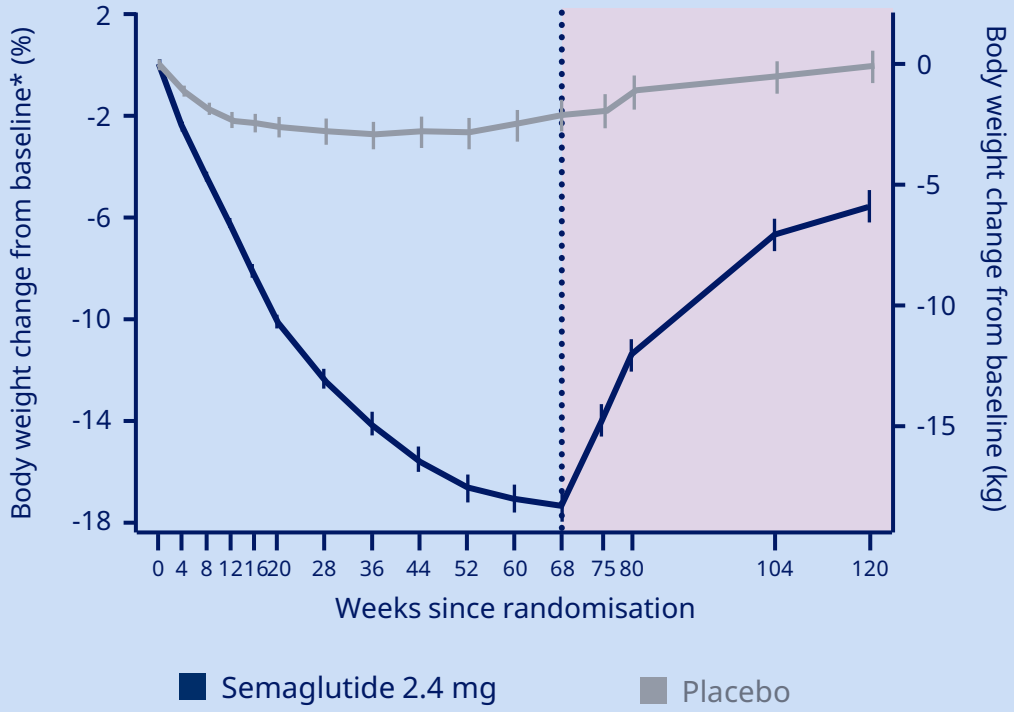
Trial product estimand: Evaluates the treatment effect under the assumption that the trial product is taken as intended

**Statistically significant vs placebo.*
BW, body weight; IBT, intensive behavioural therapy; T2D, type 2 diabetes.
Wilding JPH et al. NEJM 2021;384:989–1002; Davies M et al. Lancet 2021;10278:971–84; Wadden TA et al. JAMA 2021;325:1403–13; Rubino DM et al. JAMA 2021;14:1414–25.

Following weight loss, how would you approach the treatment of a chronic disease such as obesity?

STEP 1 extension Change in body weight

Extension analysis set mean at baseline: 105.5 kg



One year after withdrawal

After withdrawal of once-weekly semaglutide 2.4 mg and lifestyle intervention,

Participants regained approx

2/3rd

Continue therapy, like any other chronic disease

STEP 1 extension

The complementary results from STEP 4 and STEP 1-extension reaffirm **obesity** as a **chronic disease.** Like in other chronic diseases, such as hypertension or diabetes, patients with obesity require **ongoing treatment** in order to **sustain weight loss and other health benefits.**

Like hypertension or other ongoing chronic conditions, obesity requires long-term treatment

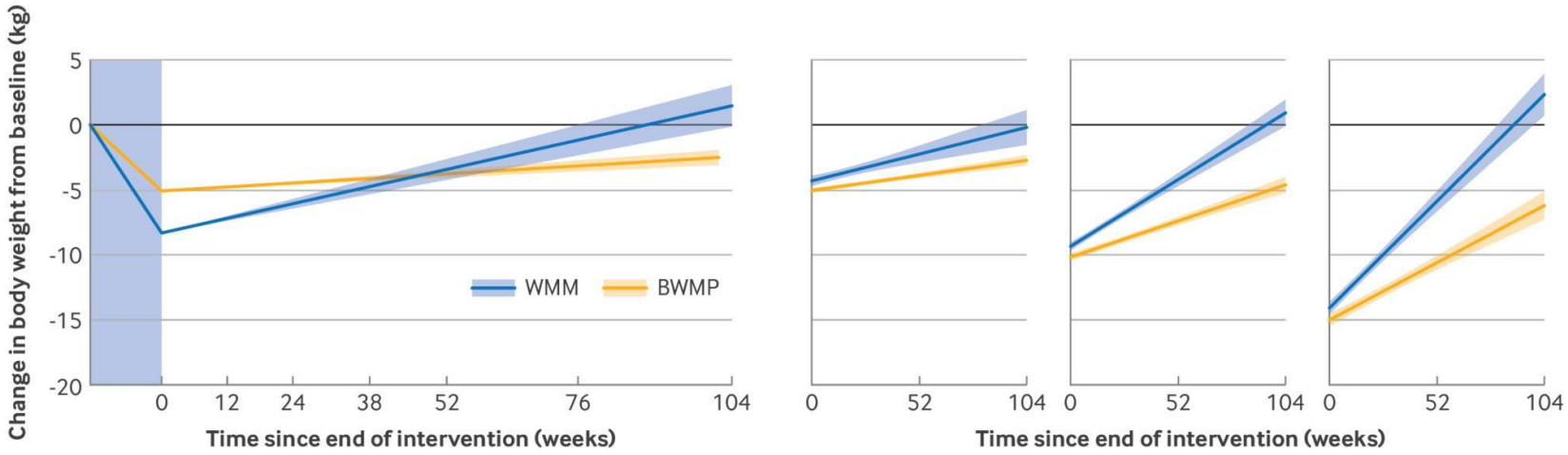
Sustained weight loss leads to health benefits and improvements in quality of life

STEP 1 extension key insights

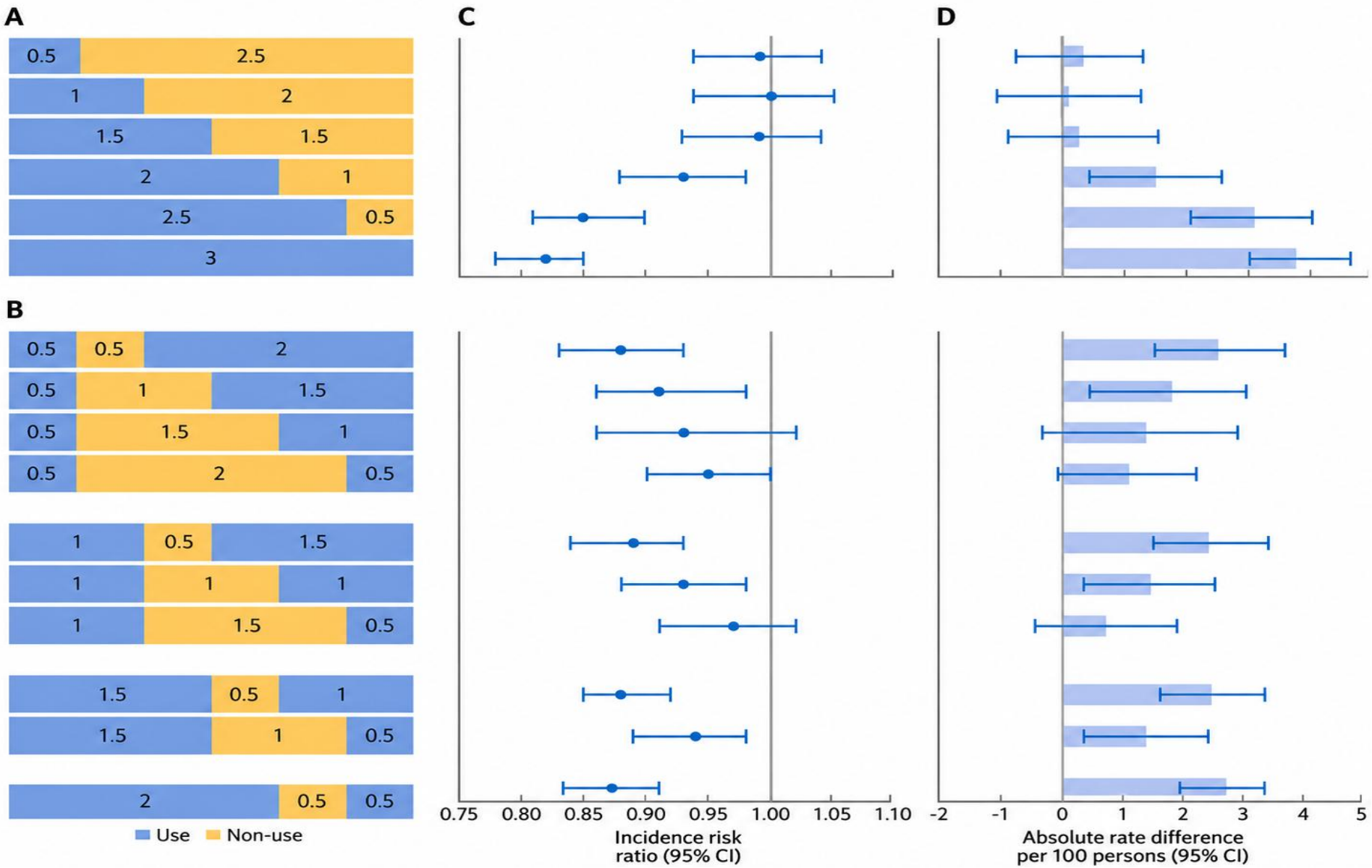
*Treatment policy estimand

1. Wilding JPH et al. Diabetes Obes Metab. 2022. doi: 10.1111/dom.14725; 2. Rubino D et al. JAMA. 2021; 325:1414–25.

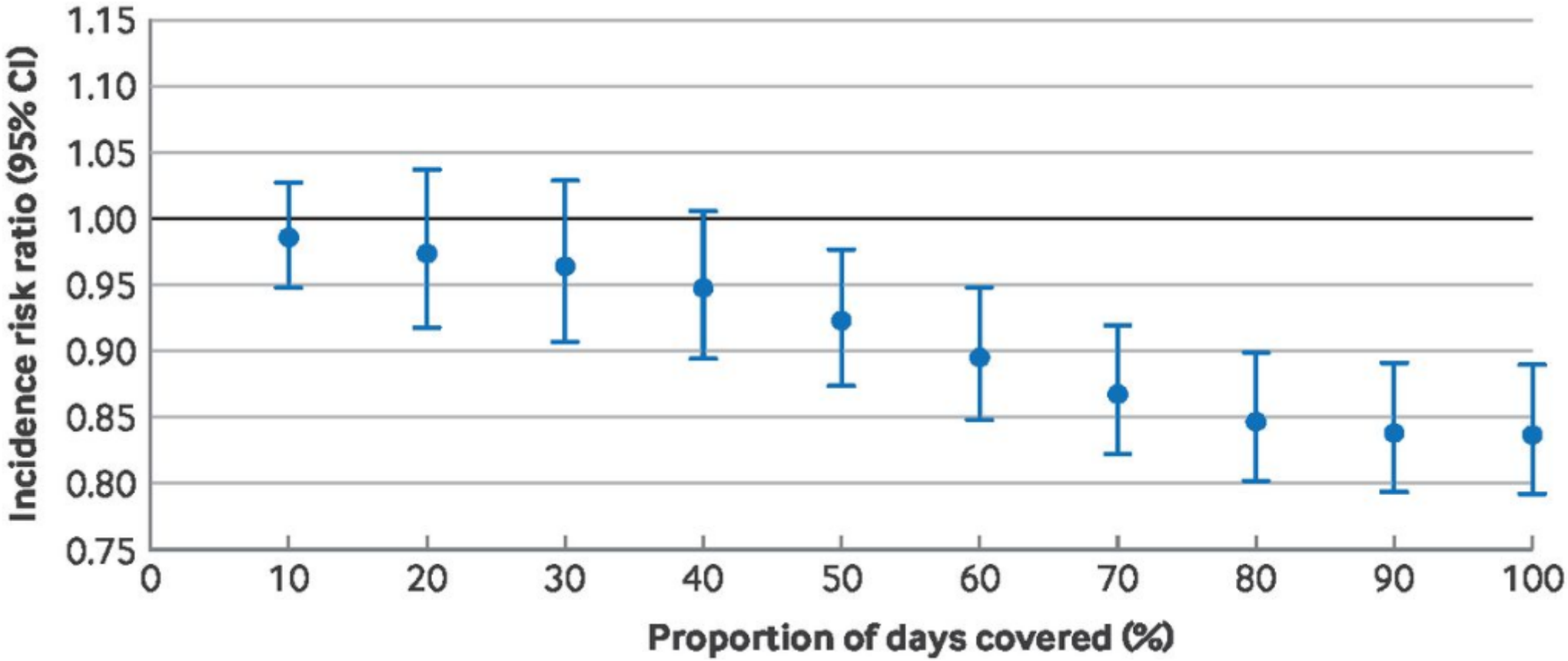
Change in body weight (kg) from baseline (treatment start) (left panel) and for a fixed amount (5 kg, 10 kg, and 15 kg) of weight loss (right panel) after treatment with WMM or BWMPs. Solid lines show weight loss during treatment (in the blue shaded area) and rate of weight regain after treatment end (95% confidence interval) estimated using mixed effects model (model 1).



Sam West et al. BMJ 2026;392:bmj-2025-085304



Xie Y, Choi T, Al-Aly Z. Glucagon-like peptide 1 receptor agonist discontinuation and risks of major adverse cardiovascular events in adults with type 2 diabetes: target trial emulation. *BMJ Medicine*. 2026;5:e002150. https://doi.org/10.1136/bmjmed-2025-002150



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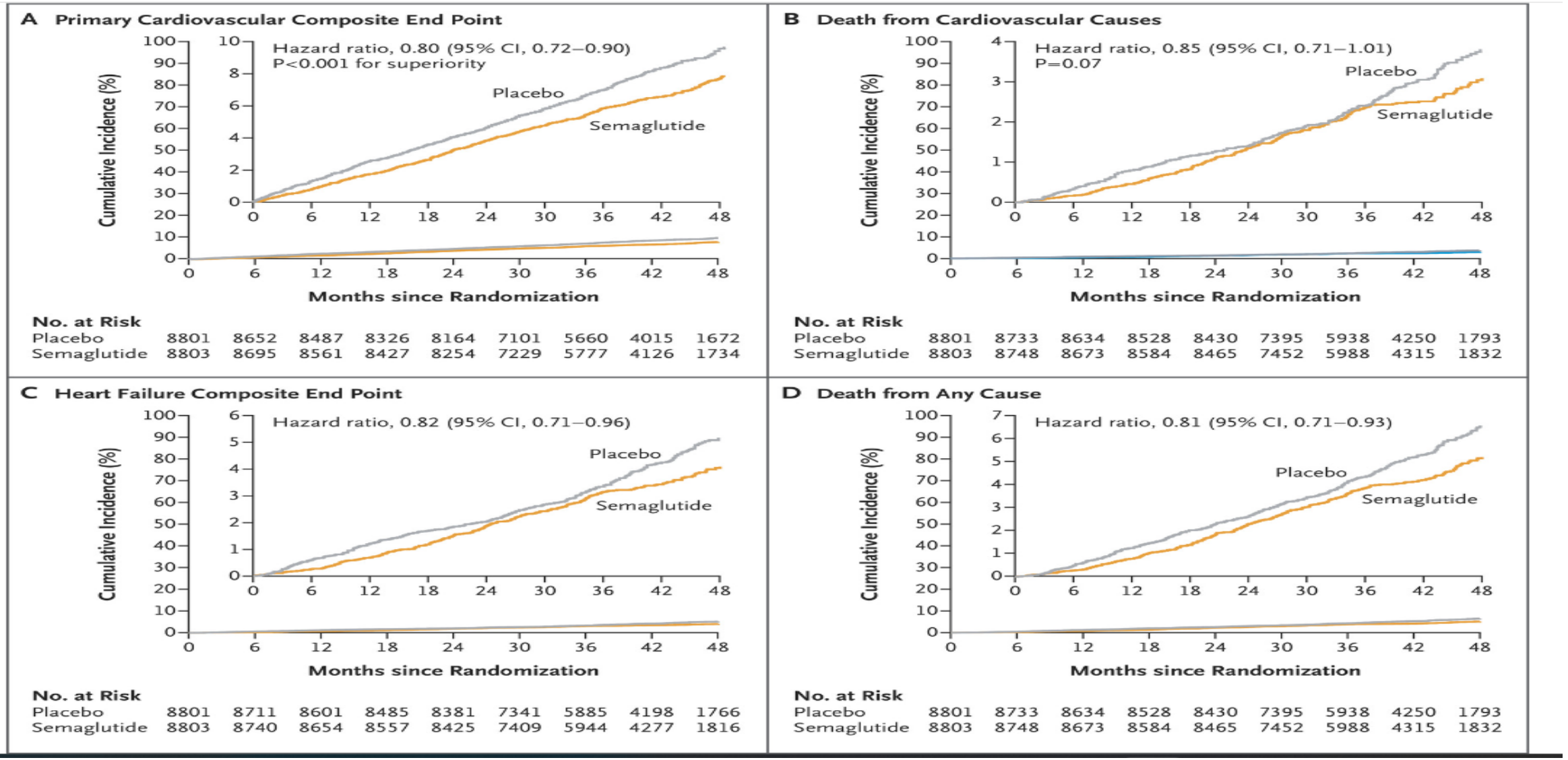
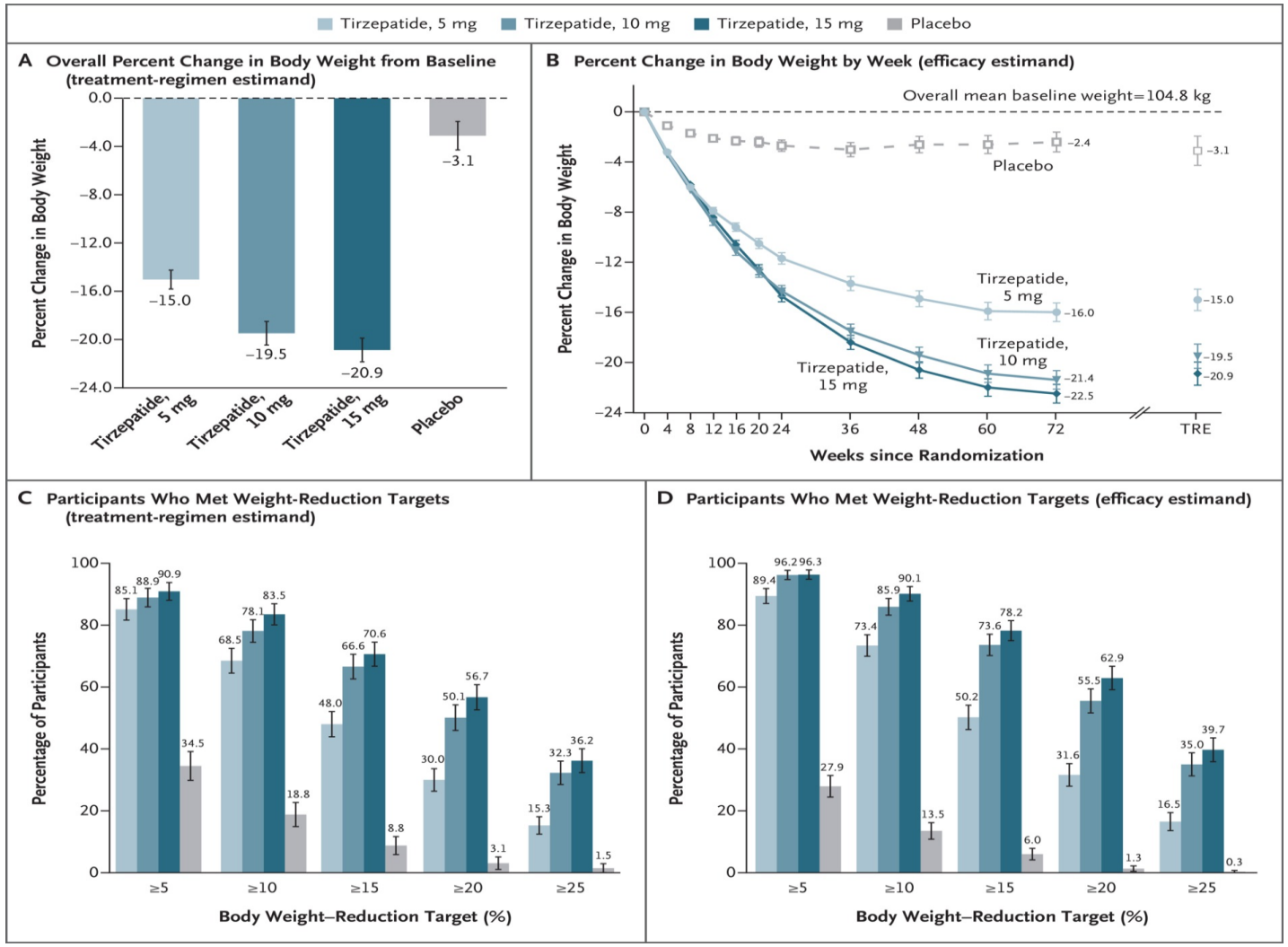
SELECT Trial



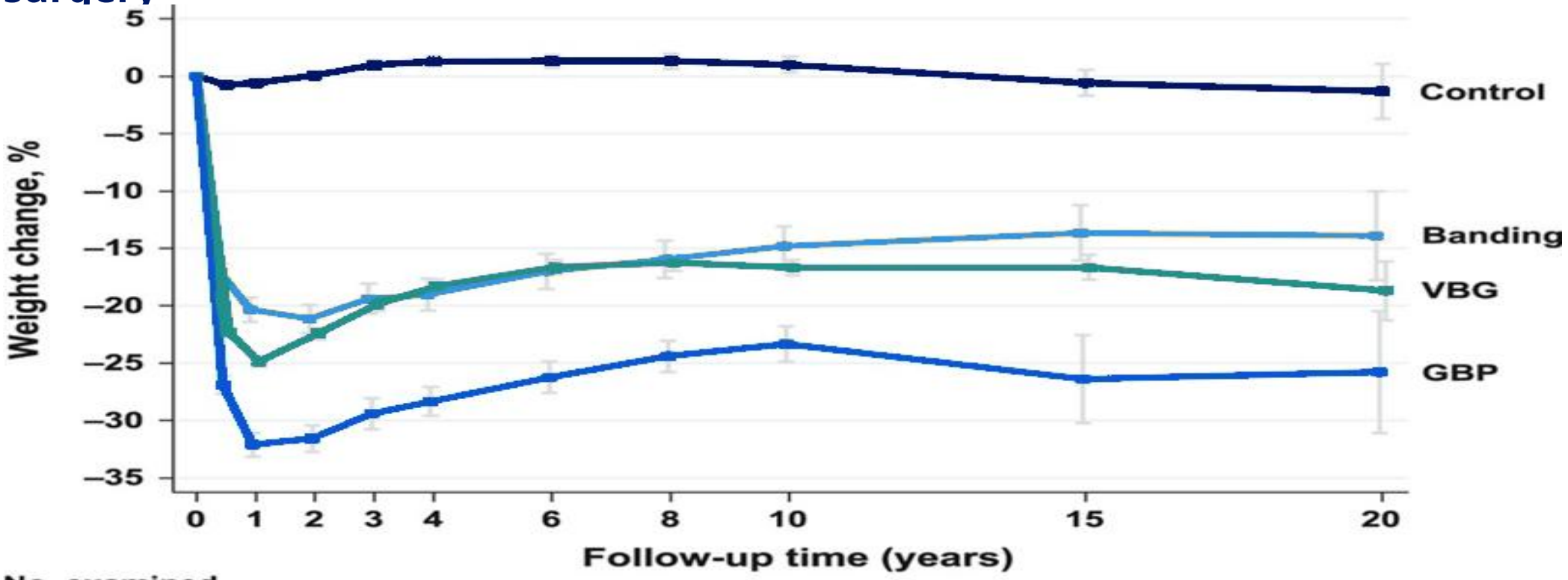
Khera Amit, Powell-Wiley Tiffany M.. (2023) SELECTing Treatments for Cardiovascular Disease — Obesity in the Spotlight. *N Engl J Med* DOI: 10.1056/NEJMe2312646.

Effect of Once-Weekly Tirzepatide, as Compared with Placebo, on Body Weight.



Jastreboff AM et al. N Engl J Med2022;387:205-216

Review of the key results from the Swedish Obese Subjects (SOS) trial – a prospective controlled intervention study of bariatric surgery



No. examined

Control	2037	1490	1242	1267	556	176
Banding	376	333	284	284	150	50
VBG	1369	1086	987	1007	489	82
GBP	265	209	184	180	37	13

Journal of Internal Medicine, Volume: 273, Issue: 3, Pages: 219-234, First published: 19 November 2012

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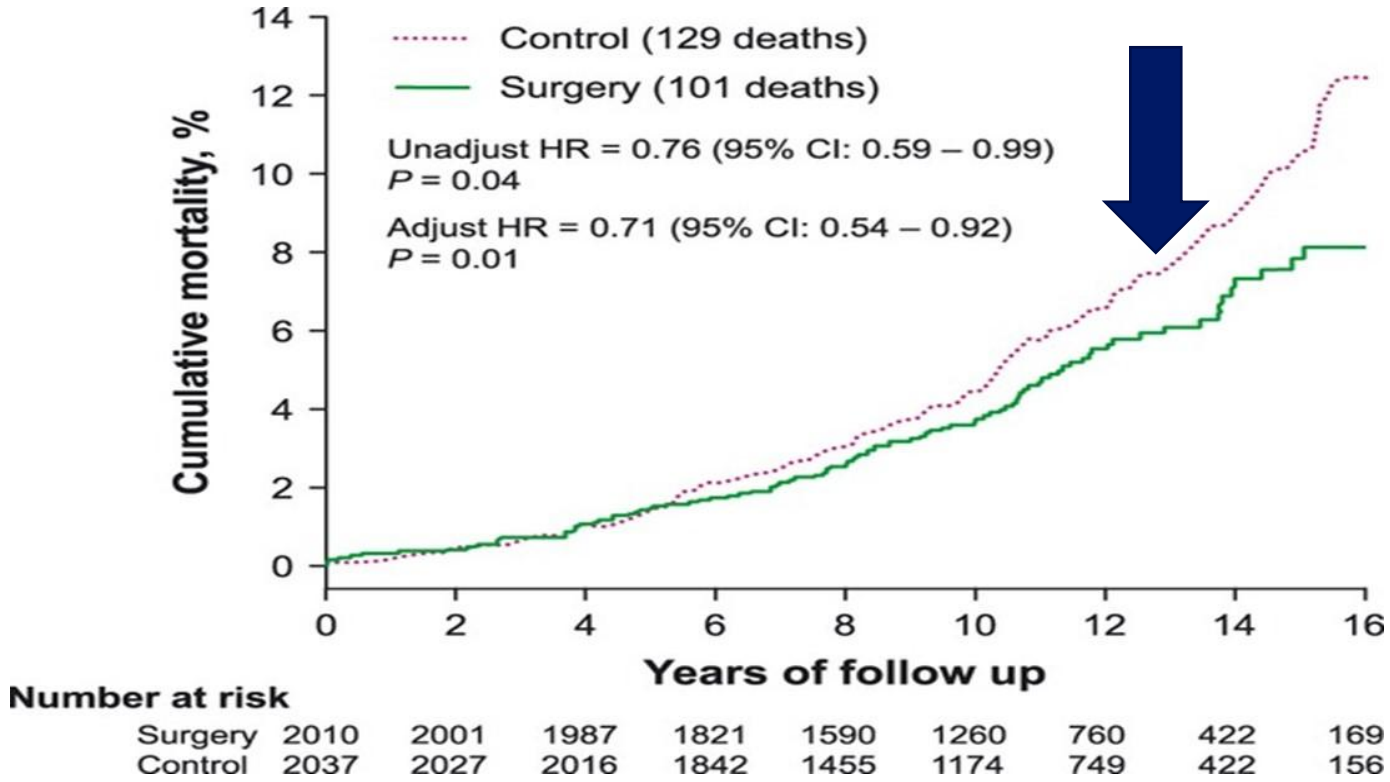
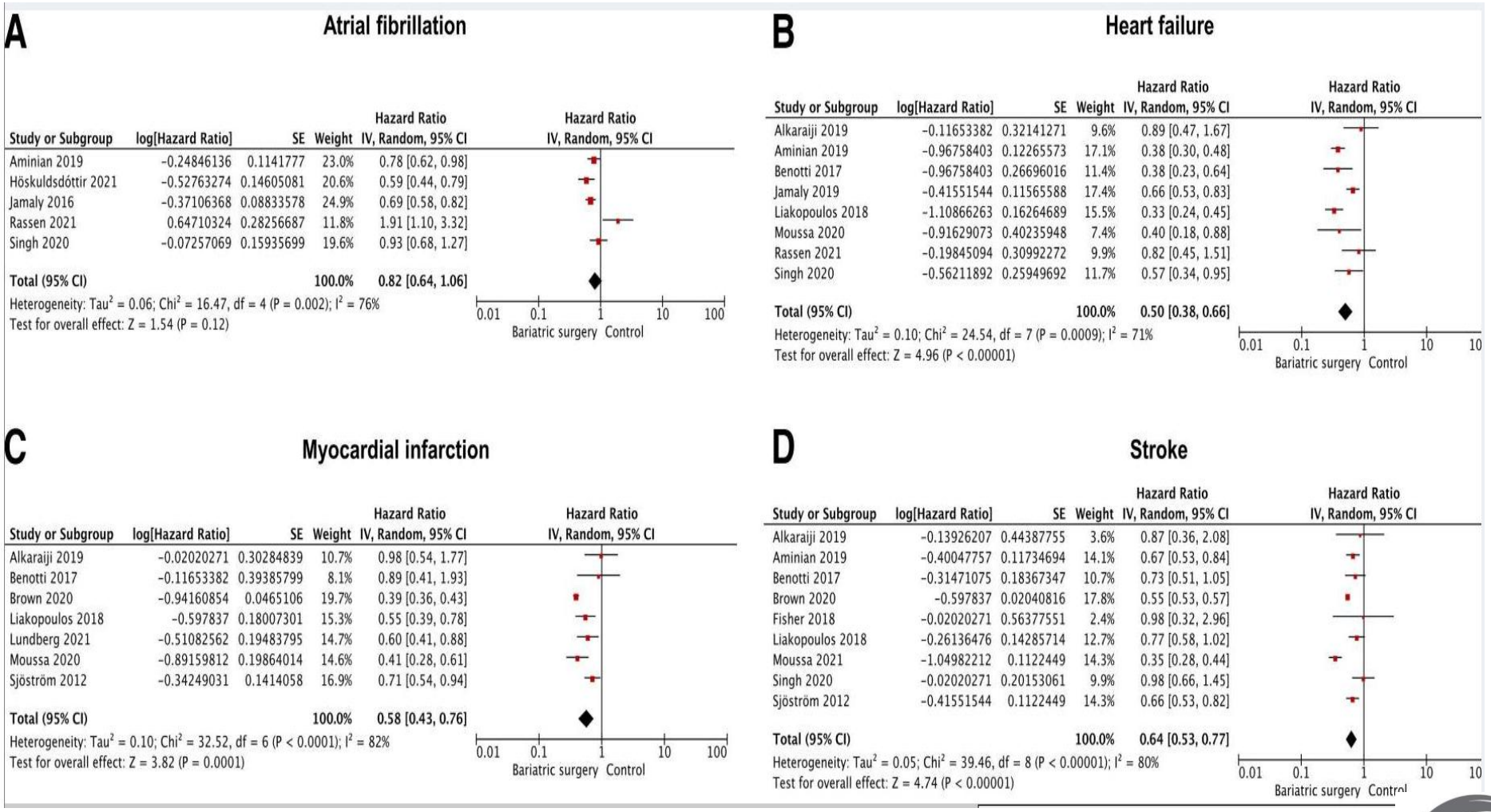


Journal of Internal Medicine, Volume: 273, Issue: 3, Pages: 219-234, First published: 19 November 2012

Cardiovascular Outcomes



van Veldhuisen, S. L., Gorter, T. M., van Woerden, G., de Boer, R. A., Rienstra, M., Hazebroek, E. J., & van Veldhuisen, D. J. (2022). Bariatric surgery and cardiovascular disease: a systematic review and meta-analysis. European heart journal, 43(20), 1955–1969

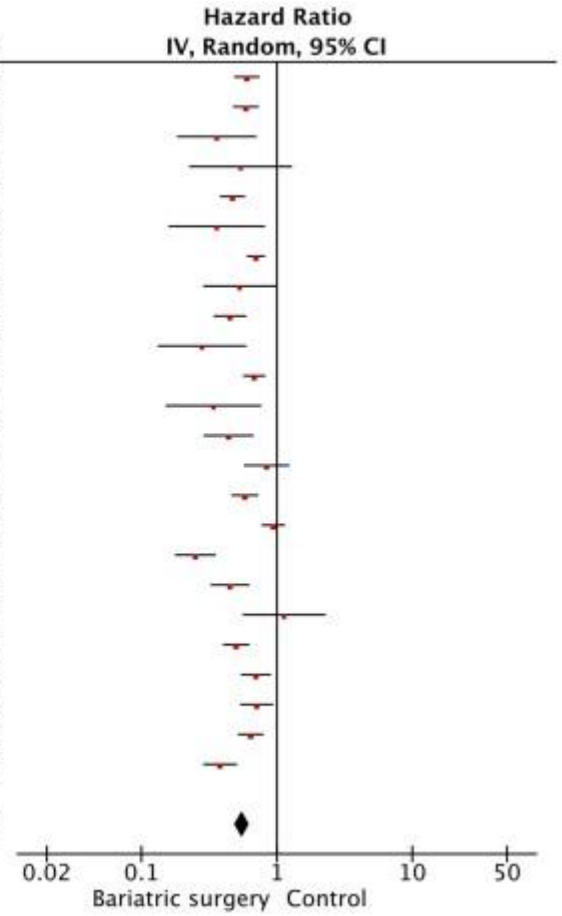
CAPE TOWN BARIATRIC CLINIC
Surgical and Medical Weight Loss Interventions

Mortality

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Adams 2007	-0.5108	0.1015383	5.5%	0.60 [0.49, 0.73]
Aminian 2019	-0.5276	0.10343498	5.4%	0.59 [0.48, 0.72]
Ardissino 2020	-1.0217	0.33628594	2.3%	0.36 [0.19, 0.70]
Arterburn 2013	-0.6162	0.43906681	1.6%	0.54 [0.23, 1.28]
Arterburn 2015	-0.755	0.10124525	5.5%	0.47 [0.39, 0.57]
Busetto 2007	-1.0217	0.4105709	1.7%	0.36 [0.16, 0.80]
Carlsson 2020	-0.3567	0.07234064	5.9%	0.70 [0.61, 0.81]
Ceriani 2019	-0.6349	0.30801407	2.5%	0.53 [0.29, 0.97]
Courcoulas 2021 (RYGB)	-0.7985	0.13321158	5.0%	0.45 [0.35, 0.58]
Courcoulas 2021 (SG)	-1.273	0.37706681	2.0%	0.28 [0.13, 0.59]
Doumouras 2020	-0.3857	0.08964232	5.6%	0.68 [0.57, 0.81]
Fisher 2018	-1.0788	0.40714666	1.8%	0.34 [0.15, 0.76]
Lent 2017 (DM2)	-0.821	0.20978544	3.7%	0.44 [0.29, 0.66]
Lent 2017 (no DM2)	-0.1744	0.18968827	4.0%	0.84 [0.58, 1.22]
Liakopoulos 2018	-0.5447	0.10880574	5.3%	0.58 [0.47, 0.72]
Lundberg 2021	-0.0619	0.09456097	5.6%	0.94 [0.78, 1.13]
Moussa 2020	-1.3863	0.16963681	4.4%	0.25 [0.18, 0.35]
Pontiroli 2020	-0.7985	0.16087419	4.5%	0.45 [0.33, 0.62]
Rassen 2021	0.1222	0.35139891	2.2%	1.13 [0.57, 2.25]
Reges 2018	-0.6931	0.10765163	5.4%	0.50 [0.40, 0.62]
Singh 2020	-0.3567	0.12278142	5.1%	0.70 [0.55, 0.89]
Sjöström 2007	-0.3425	0.13591952	4.9%	0.71 [0.54, 0.93]
Thereaux 2019 (RYGB)	-0.4463	0.10343498	5.4%	0.64 [0.52, 0.78]
Thereaux 2019 (SG)	-0.9676	0.13896101	4.9%	0.38 [0.29, 0.50]
Total (95% CI)			**100.0%**	**0.55 [0.49, 0.62]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 105.14$, df = 23 ($P < 0.00001$); $I^2 = 78\%$

Test for overall effect: $Z = 9.41$ ($P < 0.00001$)



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CONCLUSION

- Obesity is a chronic disease associated with abnormal or excess body fat that impairs health and increases mortality
- The manner in which we identify and define obesity is evolving away from the traditional BMI
- Excess weight is largely driven by excess appetite
- Treatment requires managing causes(increased appetite) and contributors at the same time
- Pharmacotherapy and metabolic and bariatric surgery are the best options for reducing appetite and for long term obesity management
- Nutritional changes along with exercise must be seen as ways to improve overall health, but not as a key strategy for weight loss

Thank you