



DR ANGELA MURPHY

Overweight and Obesity in Modern Society: Understanding the Metabolic Science, Treatment Options and Public Health Challenges

DISCLOSURES

- SPEAKER FEES from
 - Eli Lilly, Astra Zeneca, Aspen, Novo Nordisk, Merck, Novartis, Sanofi, Servier, Sandoz, Zydus
- ADVISORY BOARD
 - Pfizer, Servier, Novo Nordisk, Eli Lilly

THE DEFINITION

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

OBESITY:

- THE DISEASE NOT RECOGNIZED
- THE SCALE OF THE PROBLEM
- THE METABOLIC MELTDOWN
- THE DAMAGE BEING DONE
- THE TREATMENT:
 - A HIGH FAILURE RATE
 - THE SOLUTIONS!
- THE GUIDELINES
- THE MESSAGE TO REMEMBER

OBESITY

- THE DISEASE NOT
RECOGNIZED

OBESITY DIAGNOSIS – multiple measures

Classification	BMI (kg/m ²)	Disease risk relative to normal weight	
			Men > 102 cm Women > 88 cm
Pre-obesity	≥25 and <30	High	
Obesity			
Obesity class I	≥30 and <35	Very high	
Obesity class II	≥35 and <40	Very high	
Obesity class III	≥40	Extremely high	

WAIST TO HEIGHT RATIO

- **≥ 0.5 = obesity**
- **Independent of race, gender, age**

WAIST TO HIP RATIO

- **Men >0.90**
- **Women > 0.85**

BMI, body mass index; in, inches; NIH, National Institutes of Health; T2D, type 2 diabetes; WHO, World Health Organization.

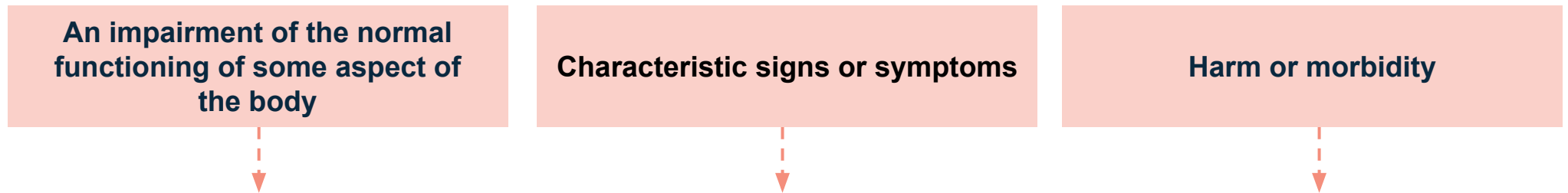
1. WHO. Waist Circumference and Waist-Hip Ratio Report: Expert Consultation, 2008. Available from

https://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf?sequence=1. Accessed March 2021; 2. NIH, National Heart, Lung and Blood Institute. Available from

https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_dis.htm. Accessed March 2021.

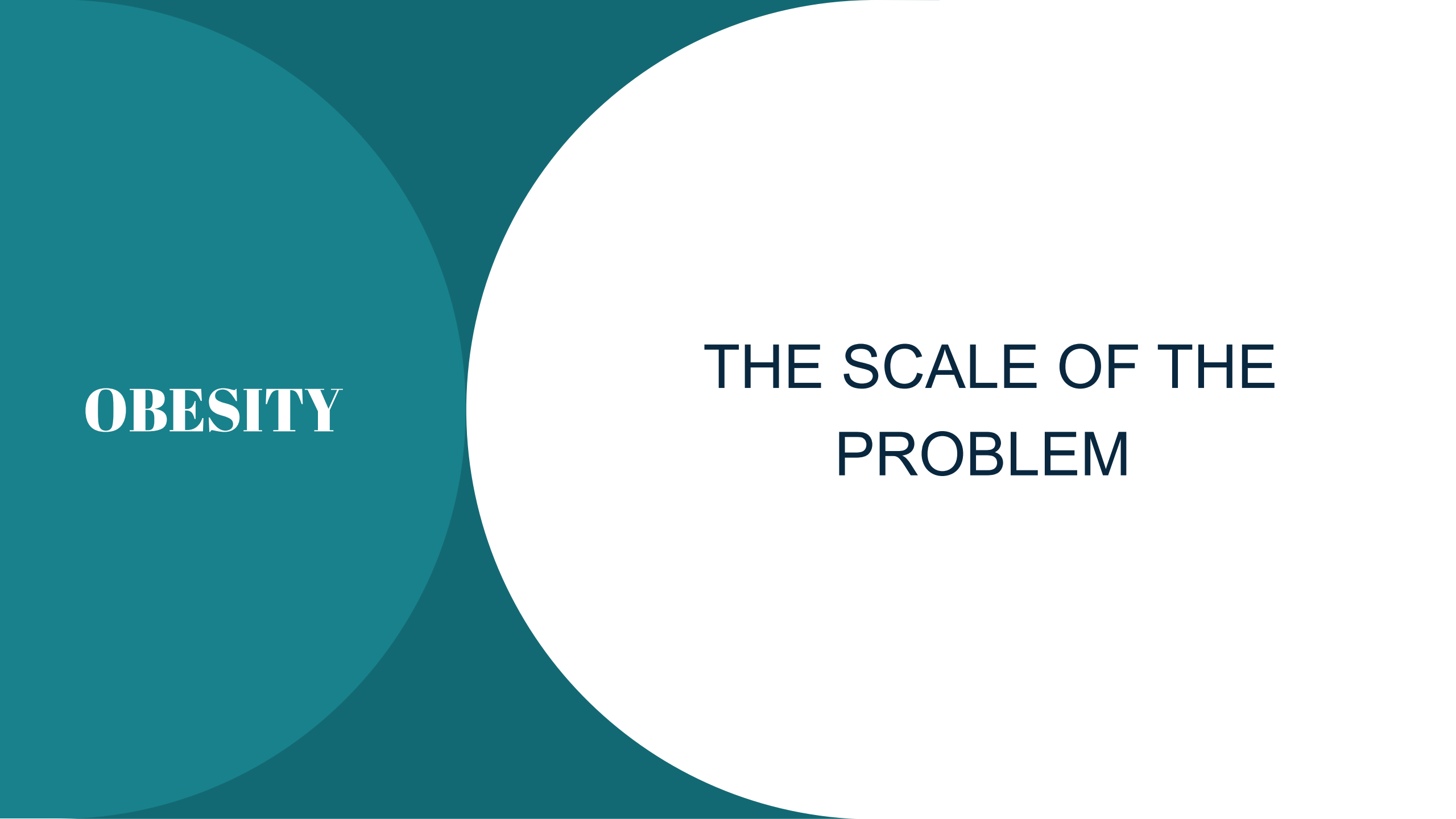
OBESITY IS A DISEASE

AMA criteria for a disease



OBESITY

1. World Health Organization. Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19–22 June 1946;
2. Mechanick et al. American Association of Clinical Endocrinologists' Position Statement on Obesity and Obesity Medicine. Endocr Pract 2012; 18(5): 642-648 .



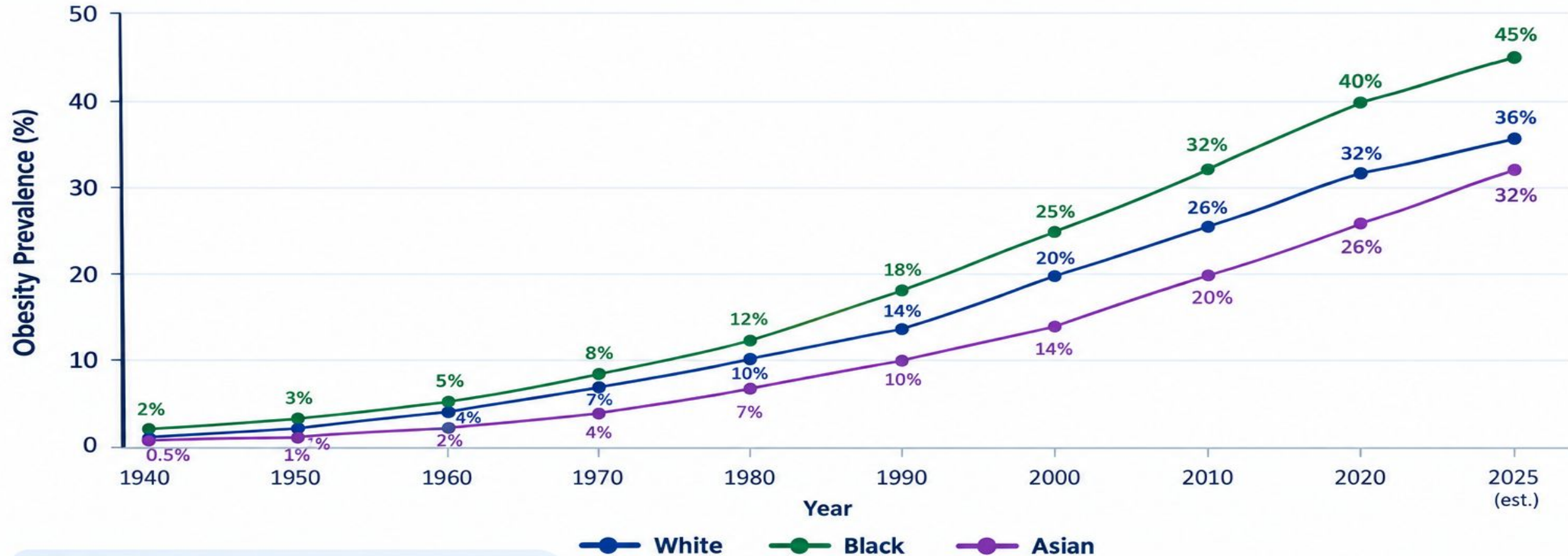
OBESITY

**THE SCALE OF THE
PROBLEM**

Global Obesity Prevalence in Different Populations

1940 – Present

Percentage of adults (aged 18+) with obesity (BMI ≥ 30 kg/m²)



Key Takeaways

- Obesity prevalence has increased in all populations since 1940, with the steepest rise from 1980 onwards.
- Black populations have consistently had the highest prevalence, followed by white populations.
- Asian populations have had the lowest prevalence, but the rate of increase has been significant, especially since 2000.

Prevalence in 2025 (est.)

45%
Black

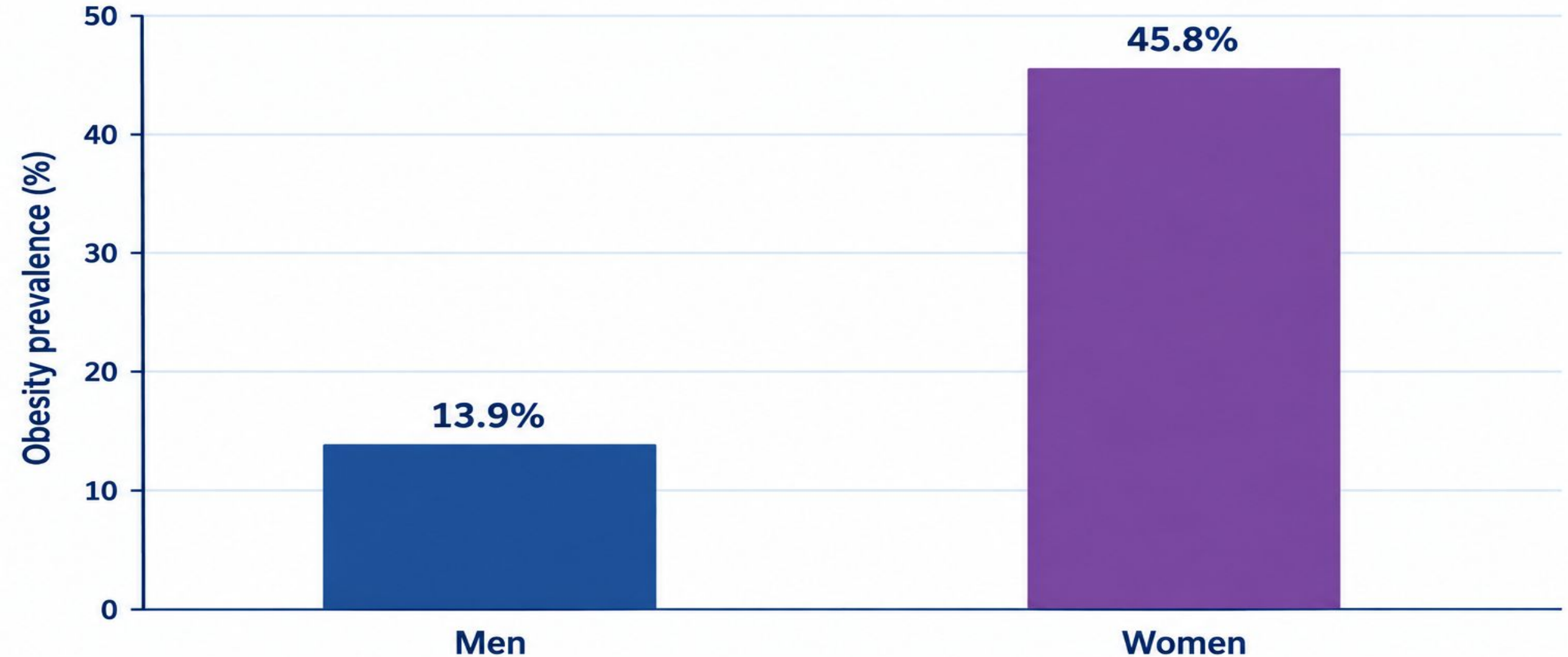
36%
White

32%
Asian

Source: WHO Global Health Observatory (2023), OECD (2023), and other population health surveys. Figures are approximate and may vary by country and survey method.

Obesity Prevalence in South African Men and Women

Age-standardized prevalence among adults aged 18+ years, 2022



Obesity defined as BMI ≥ 30 kg/m². Source: WHO / South African National Department of Health, 2022 estimates.

SOUTH AFRICA'S RISING OBESITY CRISIS (1998–2017)

Rapid growth and high prevalence across provinces and demographics.

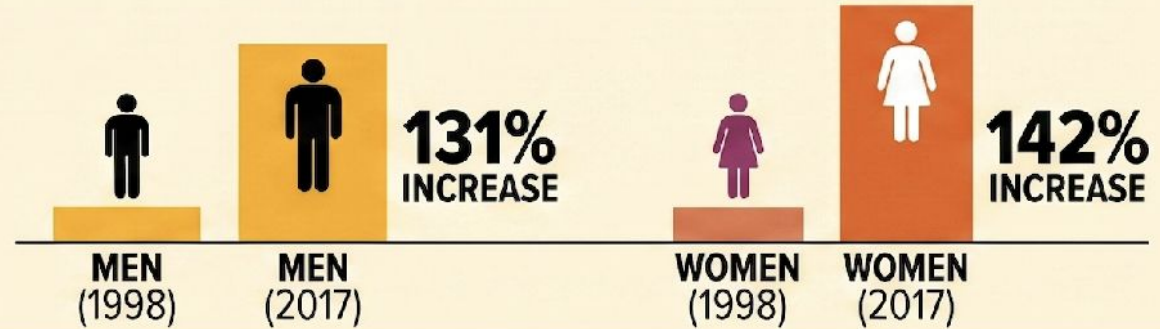
URBAN PROVINCES LEAD OBESITY RATES



40%+ ♀

Women in urbanised provinces like Gauteng and Western Cape face obesity rates exceeding 40%.

NORTH WEST PROVINCE GROWTH EXPLODES



CENTRAL OBESITY THREATENS MOST WOMEN



77.2%

Of South African women are now classified with central obesity based on waist circumference.

SIGNIFICANT URBAN-RURAL GAP IN MEN



ETHNIC DISPARITIES IN CENTRAL OBESITY



DOUBLED↑

Prevalence in Asian women.



+145%↑

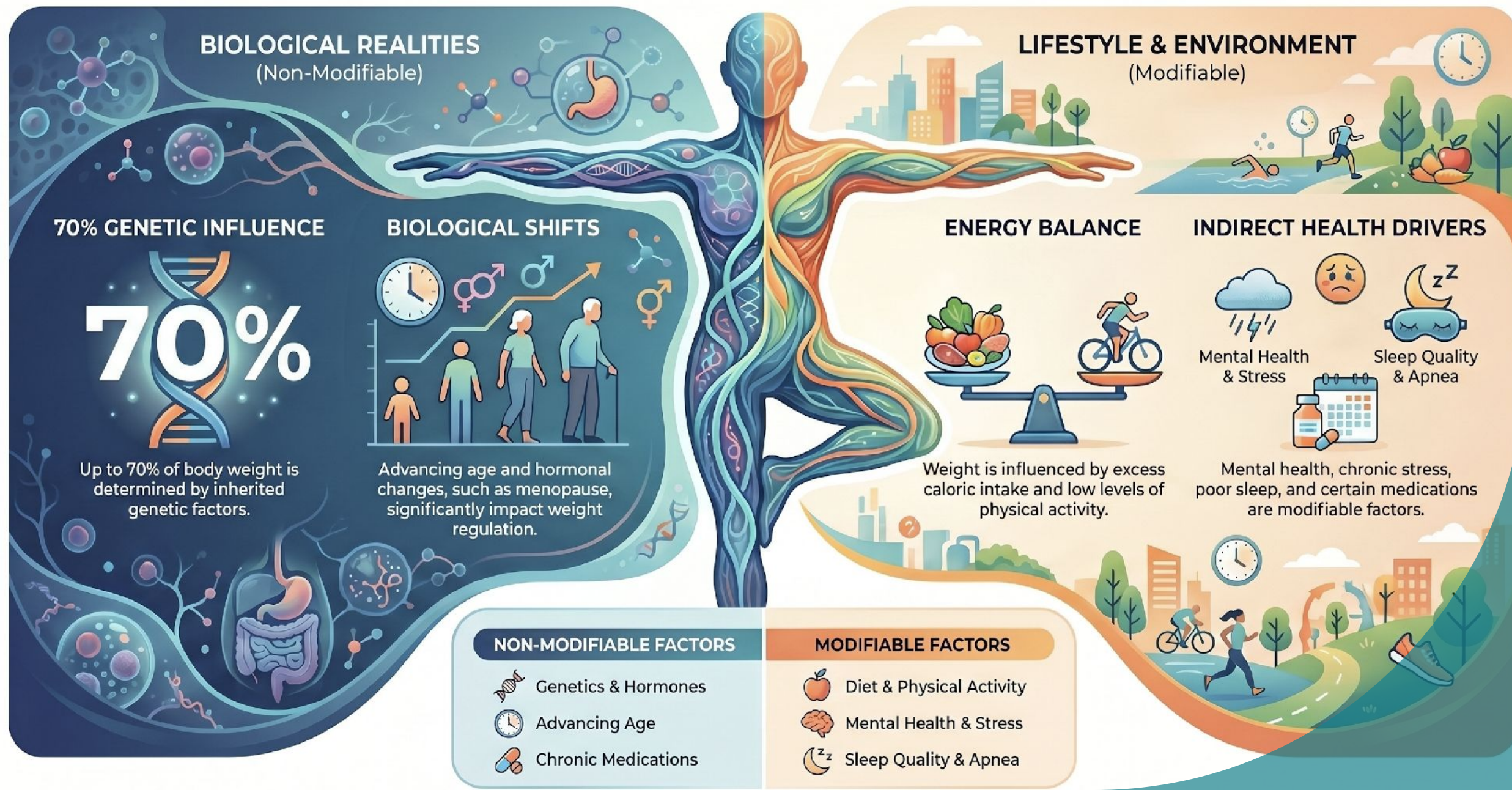
Surged in Coloured men.



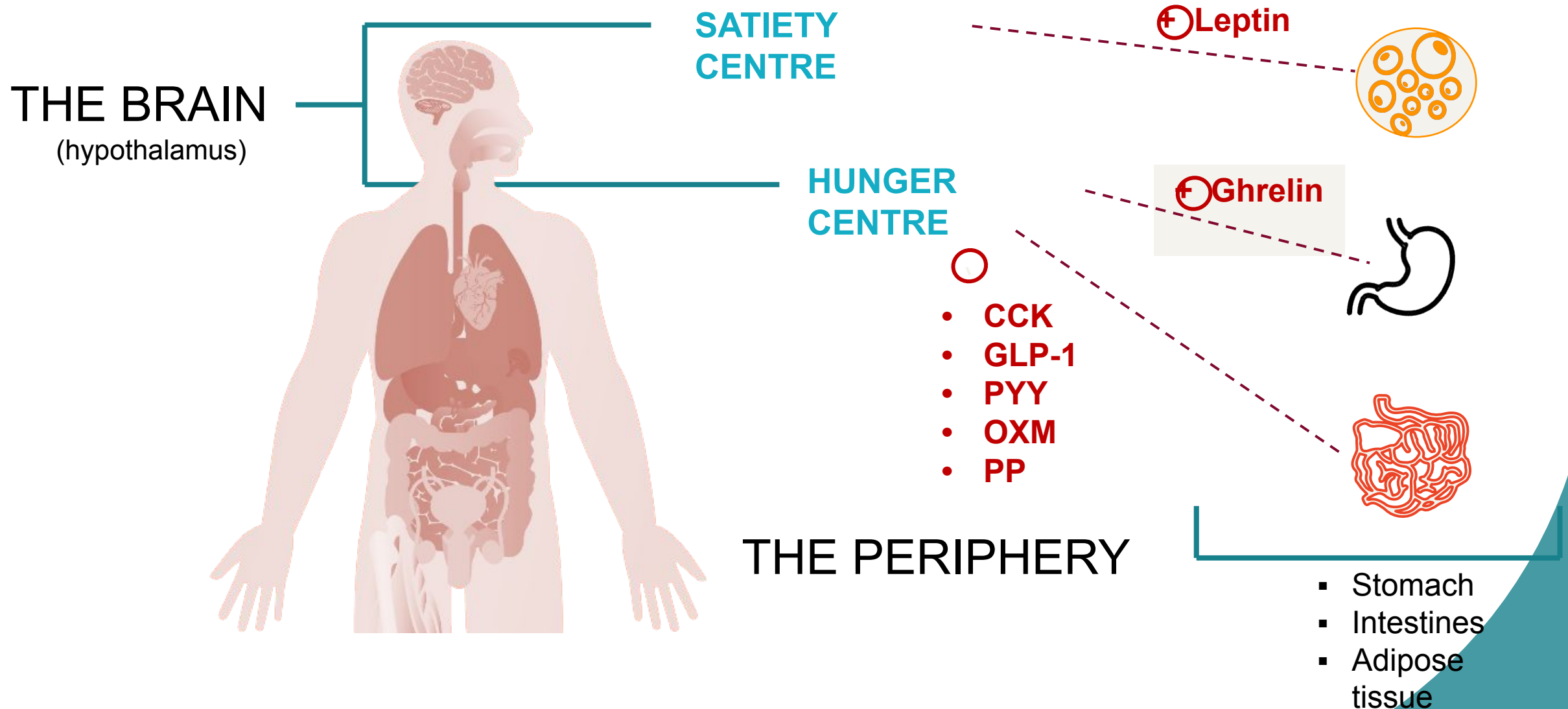
OBESITY

**THE
METABOLIC
MELTDOWN**

Beyond “You Are What You Eat”: The Complex Drivers of Obesity



energy balance: HOMEOSTATIC EATING

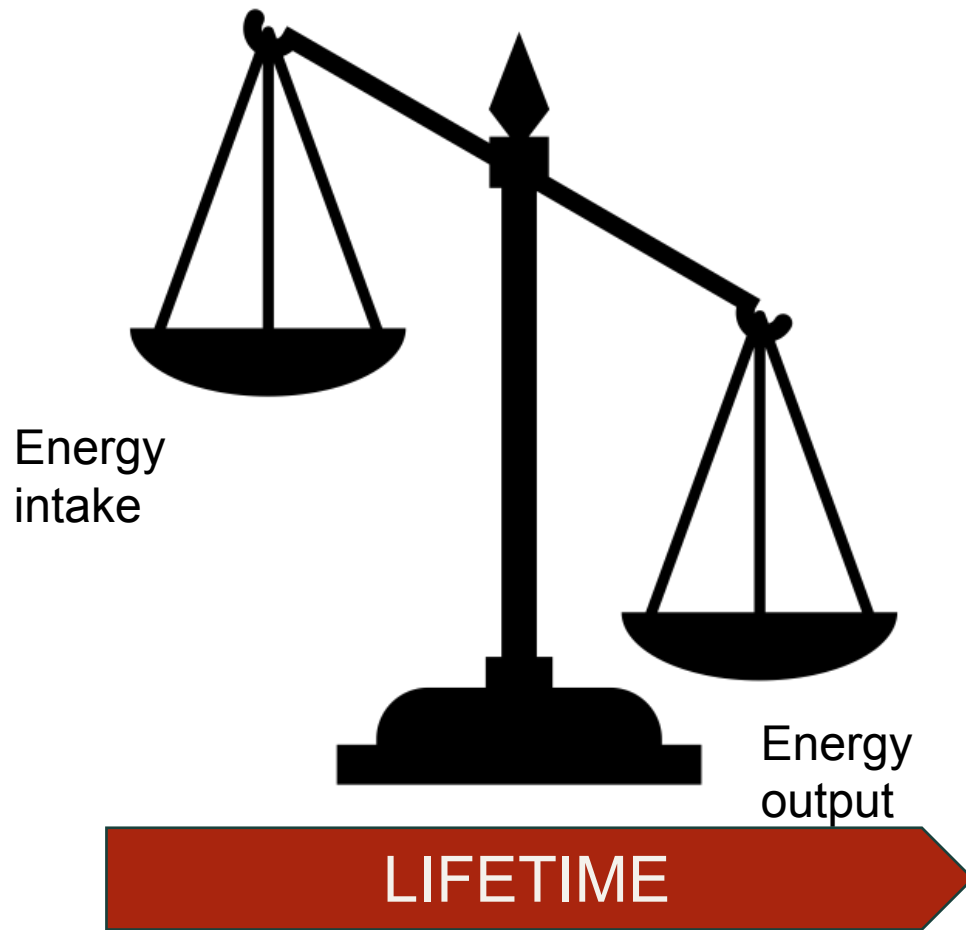


GLP-1, glucagon-like peptide-1; PP, pancreatic polypeptide; PYY, peptide YY; OXM, oxyntomodulin

1. Badman & Flier. Science 2005;307:1909–14; 2. van Bloemendaal et al. Diabetes 2014;63:4186–96; 3. Klok et al. Obes Rev 2007;8:21–34;

4. Hall et al. Am J Public Health 2014;104:1169–75.

WHAT CAUSES OBESITY?



This Photo by Unknown Author is licensed under CC BY-SA

May W, Goedecke JH, Conradie-Smit M. The science of obesity. *S Afr Med J* 2025;115(9b):e3600.

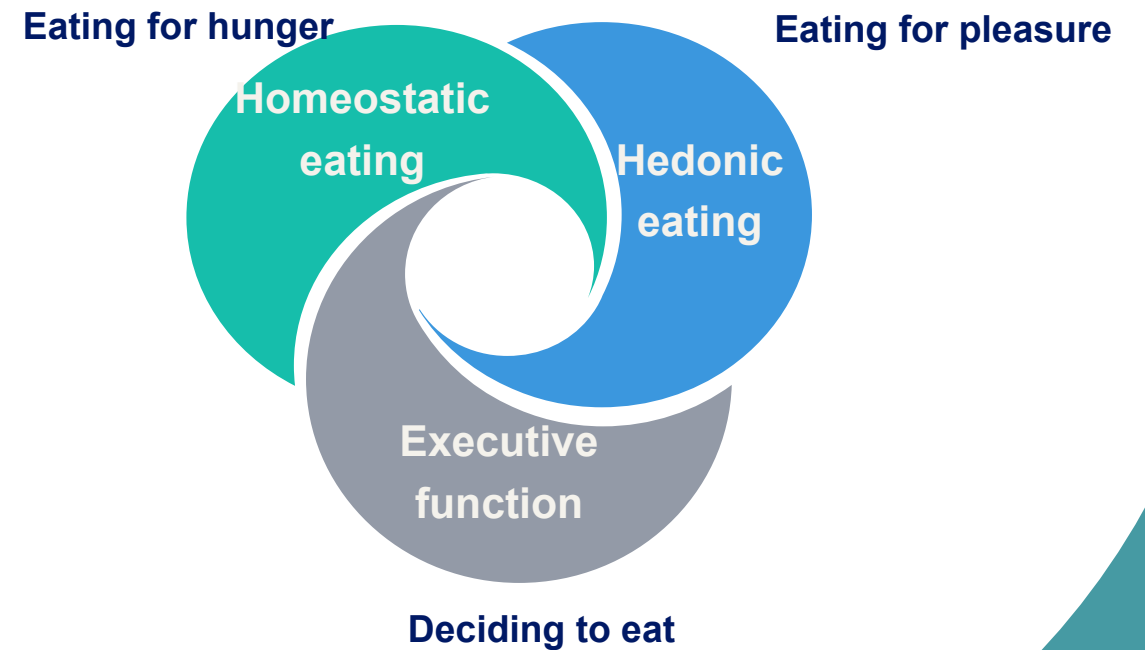
What causes obesity?

AETIOLOGY

NON-MODIFIABLE	MODIFIABLE
Genetics	Excess calories
Age	Low physical activity
Endocrine, e.g. menopause	Mental health (Stress!)
	Poor sleep
	Medications
	Endocrine, e.g. Cushing's

ENVIRONMENT

PATHOPHYSIOLOGY

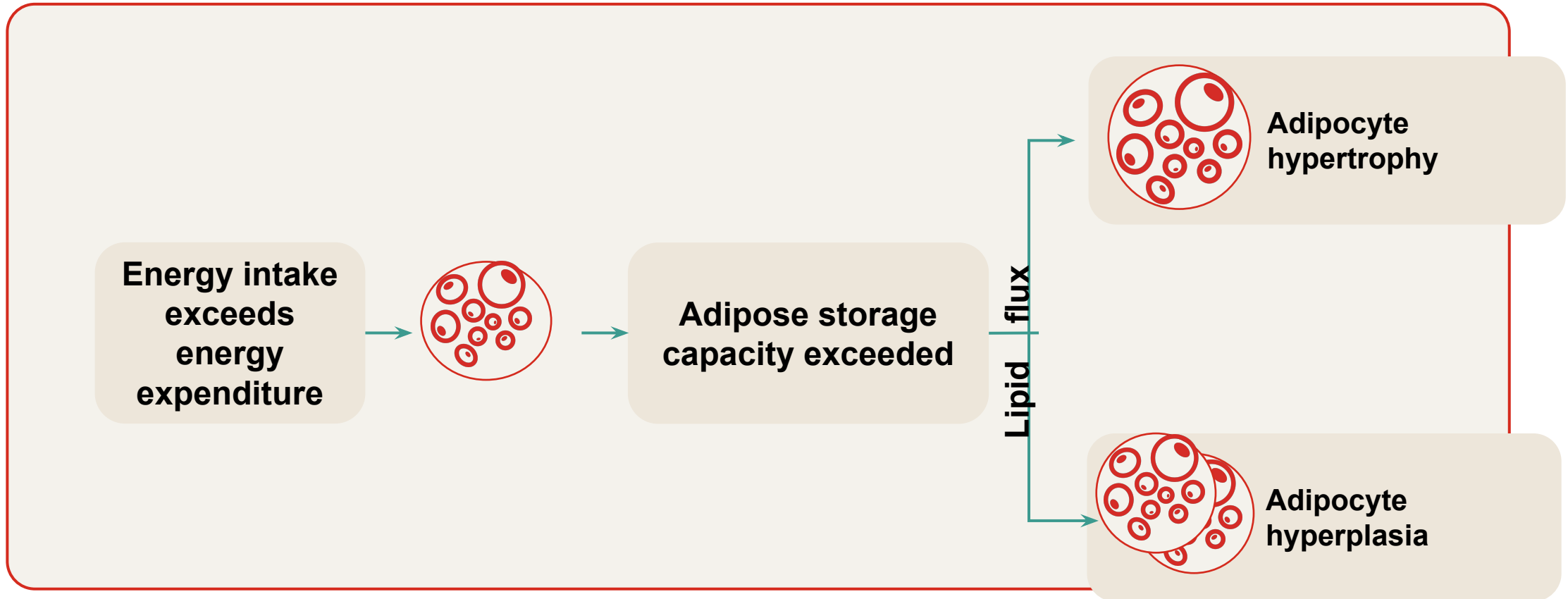




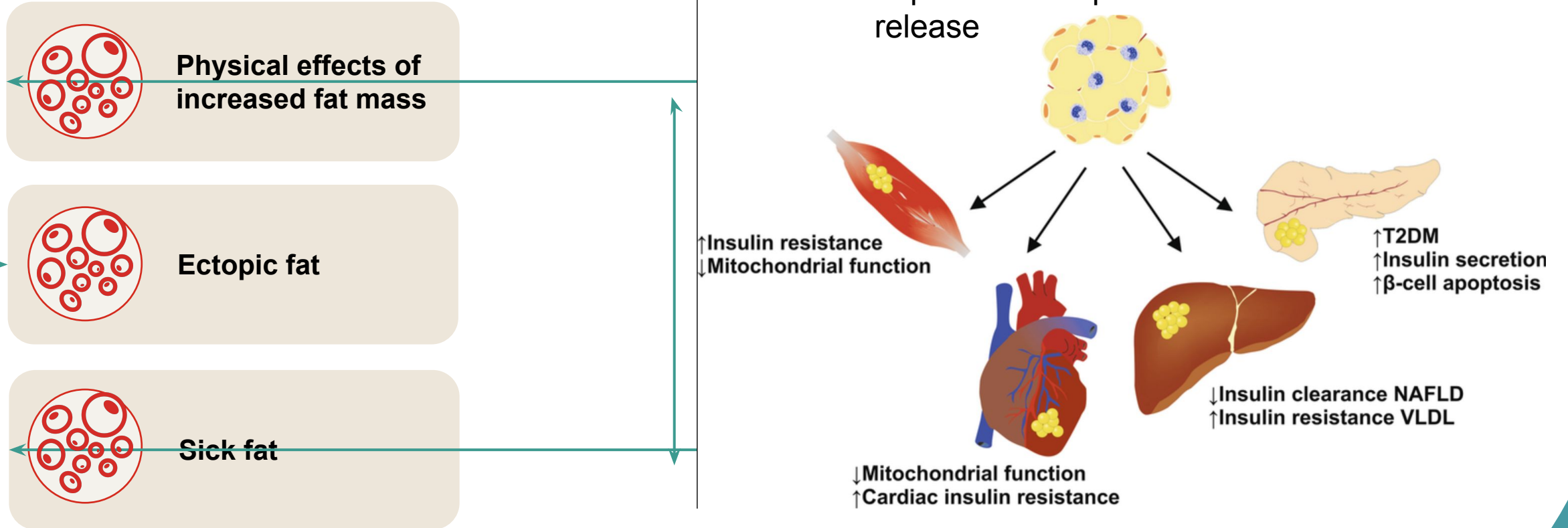
OBESITY

- THE DAMAGE BEING
DONE

WHEN FAT BECOMES 'SICK' ...



... AT ECTOPIC SITES



OBESITY COMPLICATIONS: THE 4 M's

METABOLIC



- Type 2 diabetes
- hypertension
- dyslipidaemia
- fatty liver
- cardiovascular disease
- PMOS
- cancer

MECHANICAL



- osteoarthritis
- obstructive sleep apnoea
- GERD
- incontinence
- thrombosis
- chronic pain
- poor mobility

MENTAL



- anxiety
- depression
- eating disorders
- ADHD
- addictions
- insomnia

MONETARY

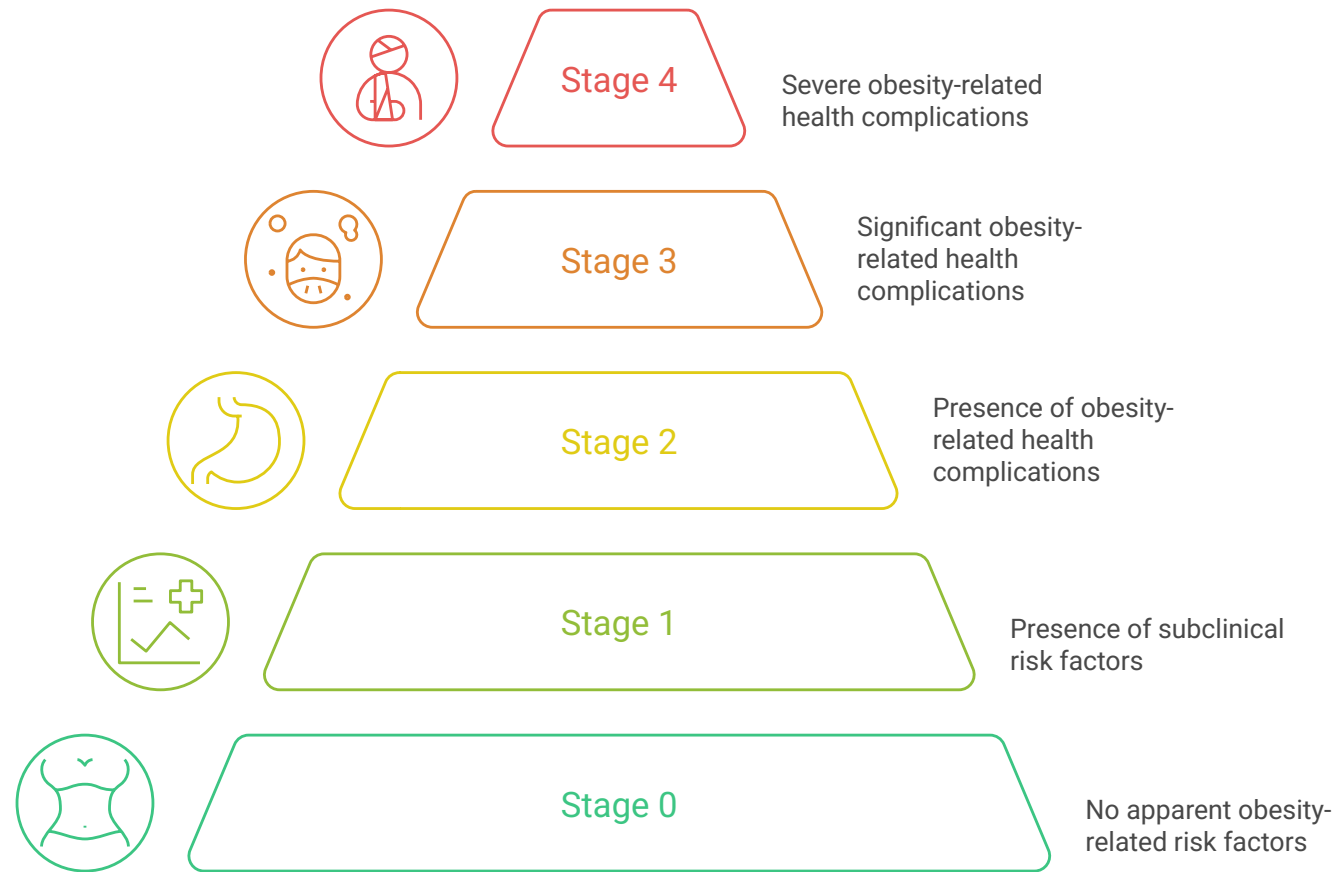


- employment
- income
- education
- access to healthcare
- disability
- insurance

OBESITY COMPLICATIONS

STAGING

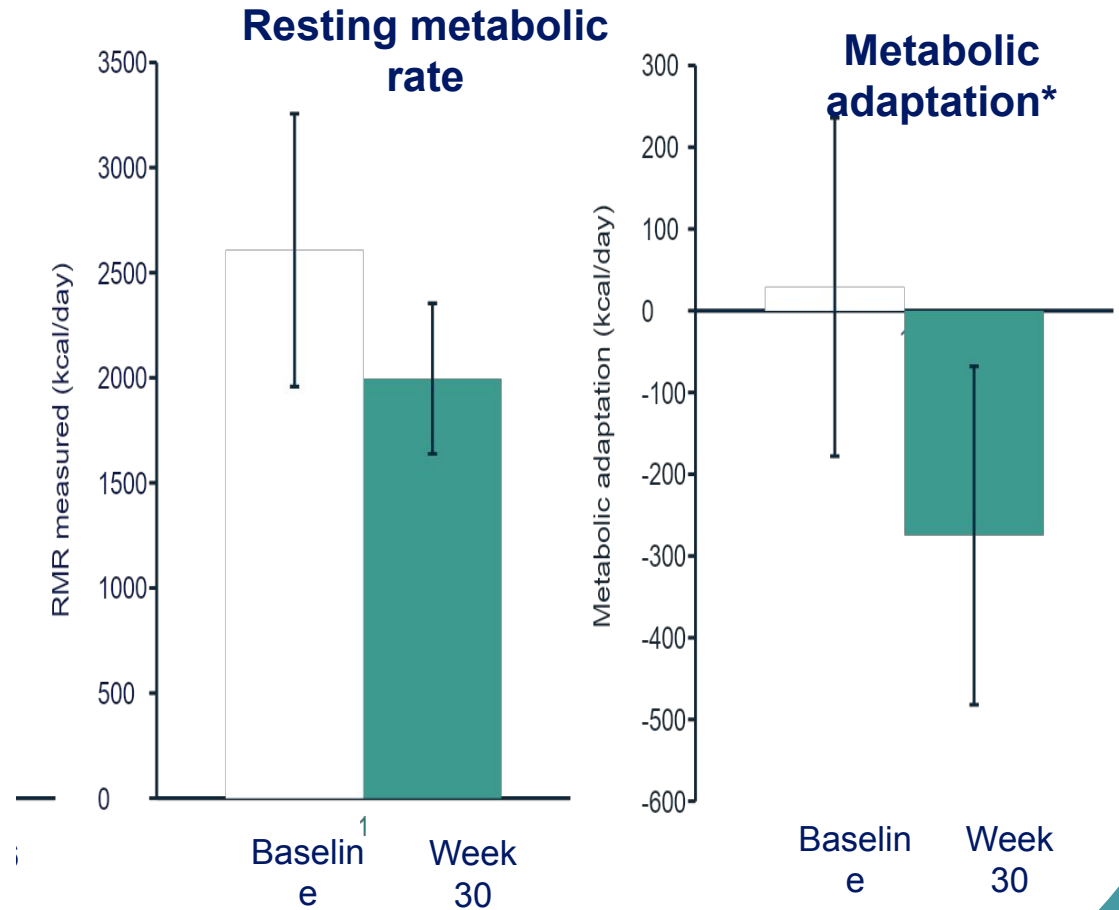
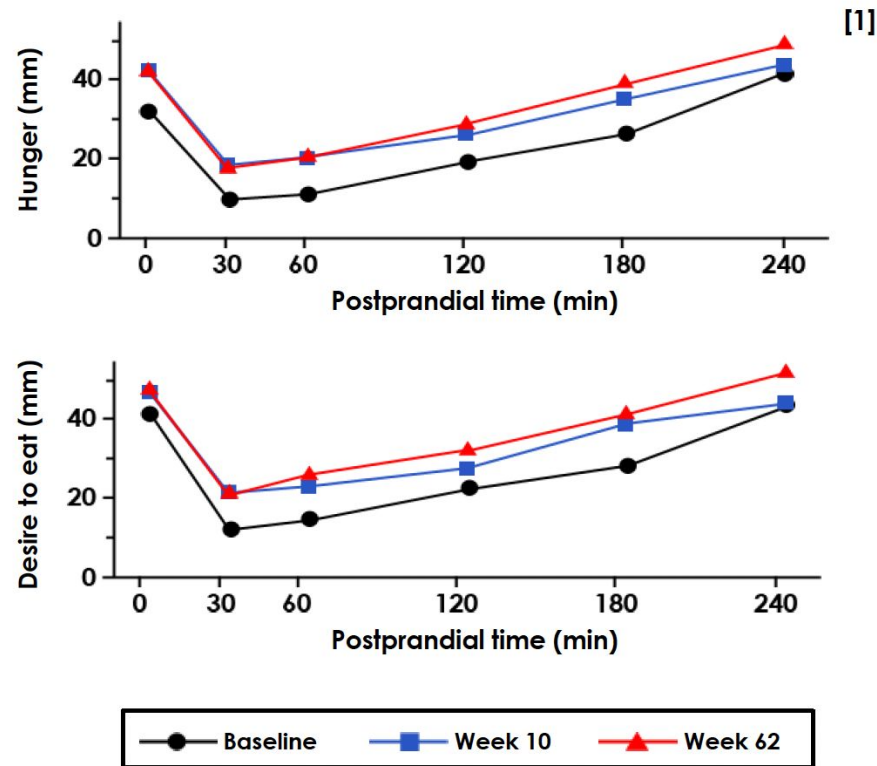
Edmonton Obesity Staging System (EOSS)



OBESITY

• **THE TREATMENT**

WEIGHT LOSS & METABOLIC ADAPTATION



58kg weight loss

Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, Proietto J. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med*. 2011 Oct 27;365(17):1597-604. doi: 10.1056/NEJMoa1105816. PMID: 22009811

Prendergast LA, et al. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. *Obesity* (Silver Spring). 2016;24:1612-1616.

STEPPED APPROACH?

BMI 25–26.9 kg/m²

BMI 27–29.9 kg/m²

BMI 30–34.9 kg/m²

BMI 35–39.9 kg/m²

BMI ≥40 kg/m²



All individuals, regardless of body size or composition, benefit from a healthy, well-balanced eating pattern and regular physical activity

BMI, body mass index.

Wharton S, et al. Obesity in adults: a clinical practice guideline. CMAJ. 2020 Aug 4;192(31):E875-E891.

Beyond Willpower:

The Biological Barrier to Weight Loss



STEPPED APPROACH?

BMI 25–26.9 kg/m²

BMI 27–29.9 kg/m²

BMI 30–34.9 kg/m²

BMI 35–39.9 kg/m²

BMI ≥40 kg/m²

Behavioral
modification



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PHARMACOTHERAPY

	MAXIMUM DOSE	MECHANISM OF ACTION	WEIGHT LOSS	SIDE-EFFECTS
<u>ORALS</u>				
ORLISTAT	120mg before meals – up to 3 times daily	Blocks fat absorption in gut	5%	Oily Stool Flatulence Malabsorption of fat-soluble vitamins
NALTREXONE/ BUPROPION	2 tablets twice daily	Reduces hunger and cravings	5%	Headache Insomnia Nausea
<u>INJECTABLES</u>				
LIRAGLUTIDE	3mg daily	GLP-1 receptor agonist – slows emptying of stomach; increases satiety	5%	Nausea, vomiting, diarrhoea or constipation
SEMAGLUTIDE	2.4mg weekly	as for liraglutide	12%	as for liraglutide
TIRZEPATIDE	15mg weekly	Dual agonist of GLP-1 and GIP receptors – slows emptying of stomach, reduces appetite	20-25%	Nausea, vomiting, diarrhoea or constipation – usually less than for GLP-1 receptor agonists

GIP AND GLP-1: IN REGULATION OF METABOLISM

GLP-1

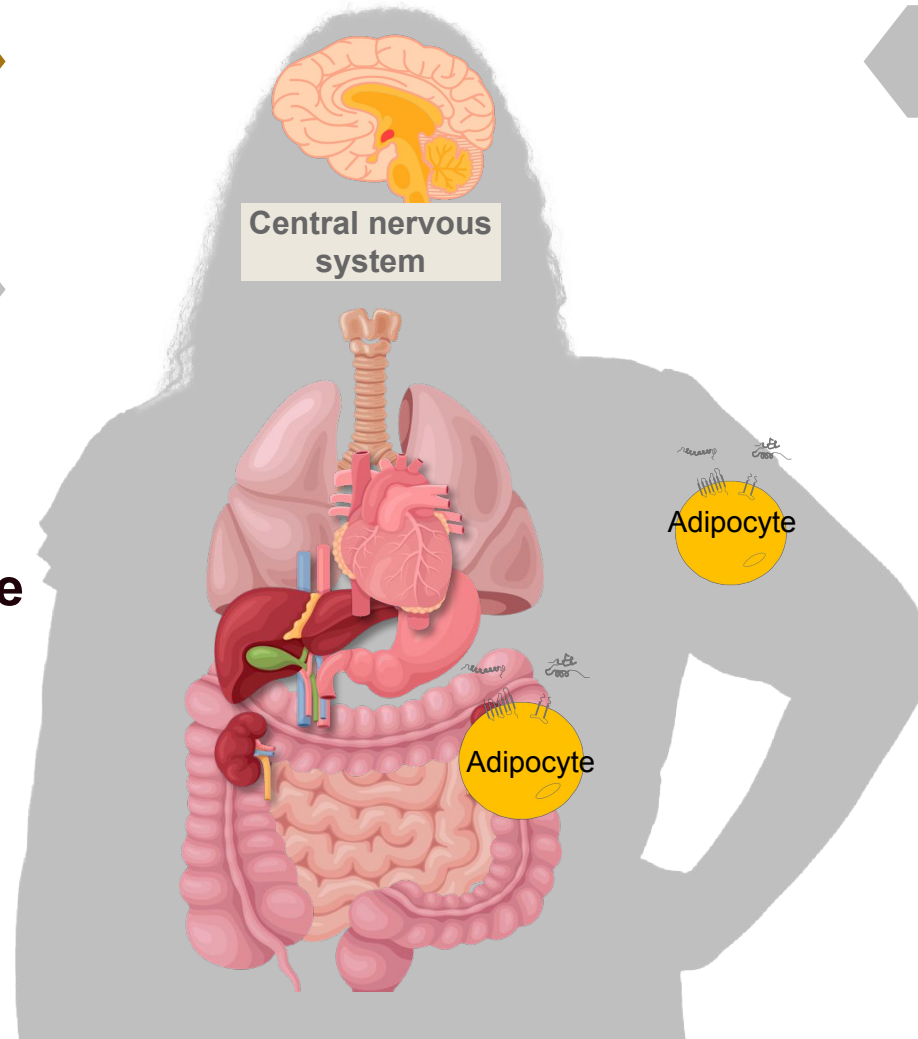


GIP activity



CENTRAL

- ❑ Reduces appetite and calorie intake
- ❑ Reduces the intensity of cravings and preferences



GIP activity

PERIPHERAL

- ❑ Regulates glucose uptake
- ❑ Modulates lipid uptake

GLP-1/GIP THERAPIES: MITIGATING SIDE-EFFECTS

MEALS

- Smaller
- Chew well
- Avoid fatty foods
- Drink water

NUTRIENTS

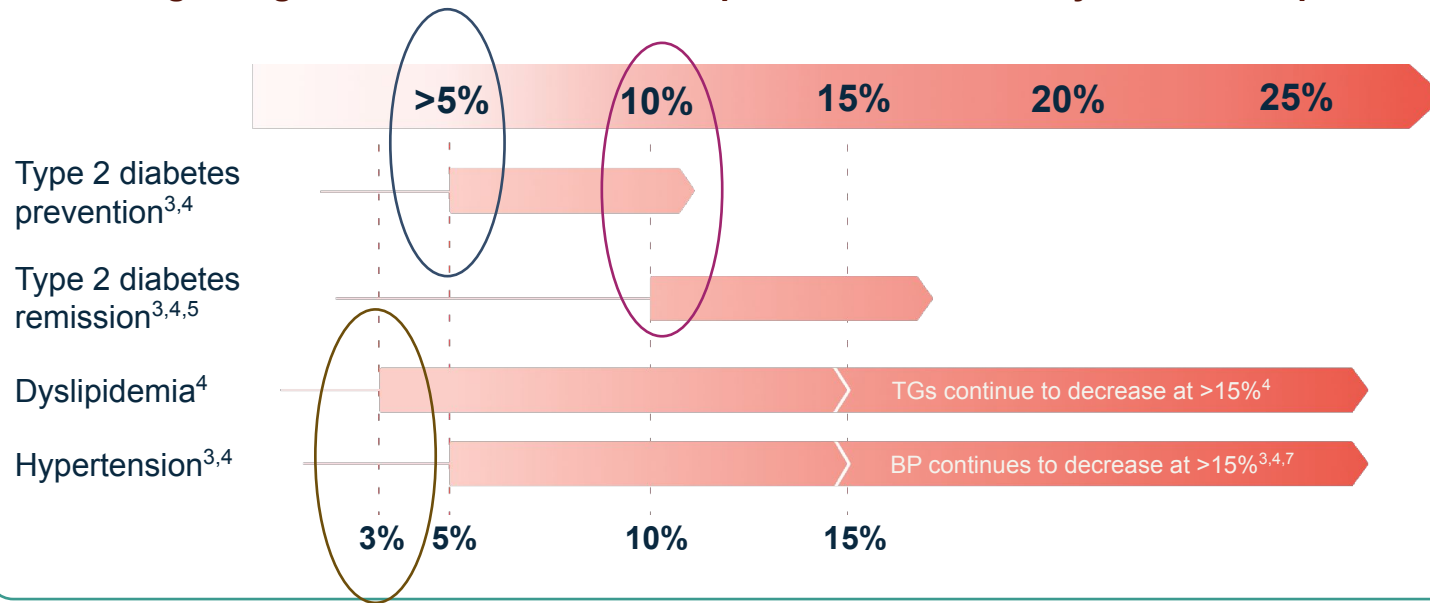
- Protein
- Fibre
- Micronutrients
- Fluids

MEDICATIONS

- May need to stop metformin
- May need non-OCP contraception
- Inform anaesthetist

THE EFFECTS OF WEIGHT LOSS

Percentage weight loss associated with improvements in Obesity-related complications



- **Diabetes Prevention Program**
- **Finnish Diabetes Prevention Study Group** ed complications^{3,6,7}
- **DiRECT Trial** ed complications^{3,6,7}
- **Wadden et al.** ed complications^{3,6,7}

BP, blood pressure; **CV**, cardiovascular; **CVD**, cardiovascular disease; **TG**, triglyceride.

1. Haase CL, et al. Int J Obes (Lond). 2021;45(6):1249–58. 2. Handelsman Y, et al. J Diabetes Complications. 2023;37(2):108389. 3. Horn DB, et al. Postgrad Med. 2022;134(4):359–75. 4. Garvey WT, et al. Endocr Pract. 2016;22(Suppl 3):1–203. 5. Lean ME, et al. Lancet. 2018;391(10120):541–51. 6. Garvey WT. J Clin Endocrinol Metab. 2022;107(4):e1339–e47. 7. Cefalu WT, et al. Diabetes Care. 2015;38(8):1567–82. 8. Powell-Wiley TM, et al. Circulation. 2021;143(21):e984–e1010. 9. Lopez-Jimenez F, et al. Eur J Prev Cardiol. 2022;29(17):2218–37. 10. Hritani R, et al. Obes Pillars. 2023;7:100069.

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

- Adapted from Canadian Adult Obesity Clinical Practice Guideline
- Incorporated local research, needs and resource availability
- Eighteen chapters covering
 - Science of obesity
 - Patient-centred non-stigmatizing care
 - Recognize Obesity as a chronic disease
 - Assessment of patients living with obesity
 - Treatment strategies to reduce the complications of obesity
 - Medical Nutrition Therapy
 - Physical activity
 - Pharmacotherapy
 - Surgery

<https://samajournals.co.za/index.php/samj/issue/view/149>

The Patient Mandate: Releasing the stigma and embracing comprehensive care.

1

Acknowledge the Biology.

Obesity is not a failure of willpower; it is a chronic condition.

2

Utilize Available Tools.

Safe and effective obesity medications are available beyond lifestyle alone.

3

Focus on the Holistic Goal.

Medications facilitate management of complications, achieve meaningful weight reduction, and critically improve quality of life.



The Provider Mandate: Sustaining treatment and optimizing the clinical environment



Commit to the Long-Term

Obesity medications are safe and effective when used long-term; care must be sustained and comprehensive.



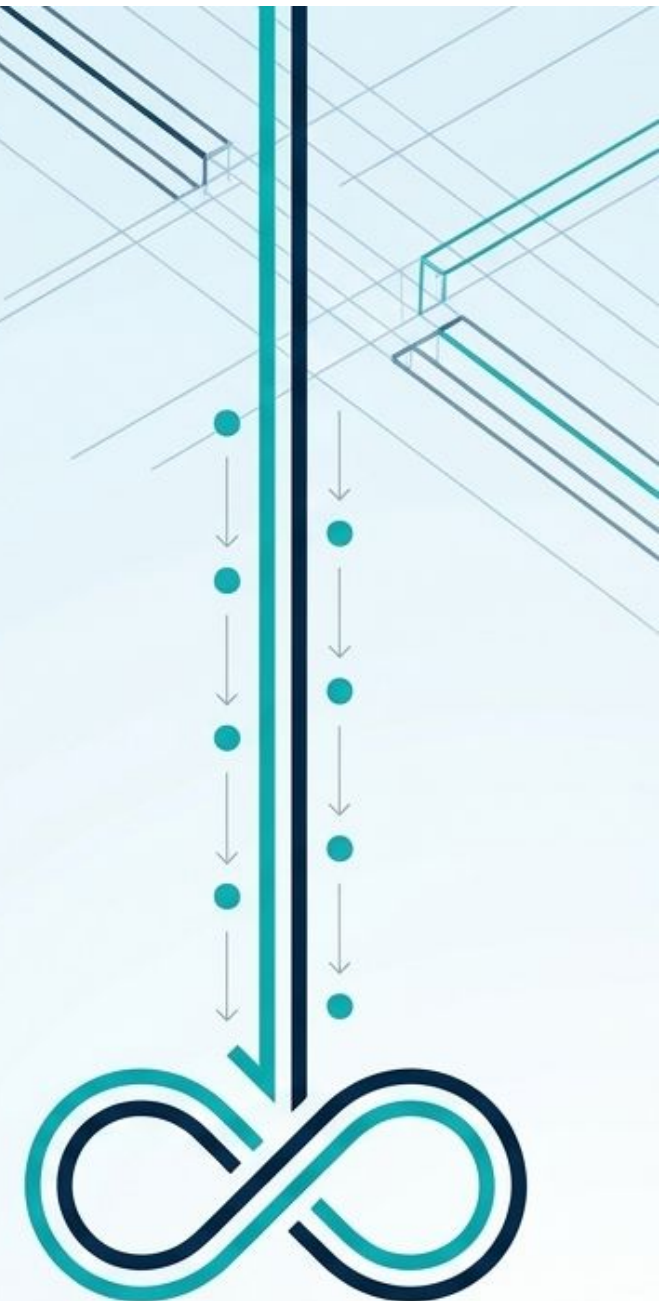
Prevent Discontinuation

Avoid stopping medications without medical cause (like pregnancy or severe side effects) to prevent treatment failure.



Redefine the Clinical Environment

Obesity care must be collaborative, individualized, accessible, and completely stigma-free.



The Policy Mandate: Guaranteeing equitable access at the population level

Recognize Essential Therapeutics.

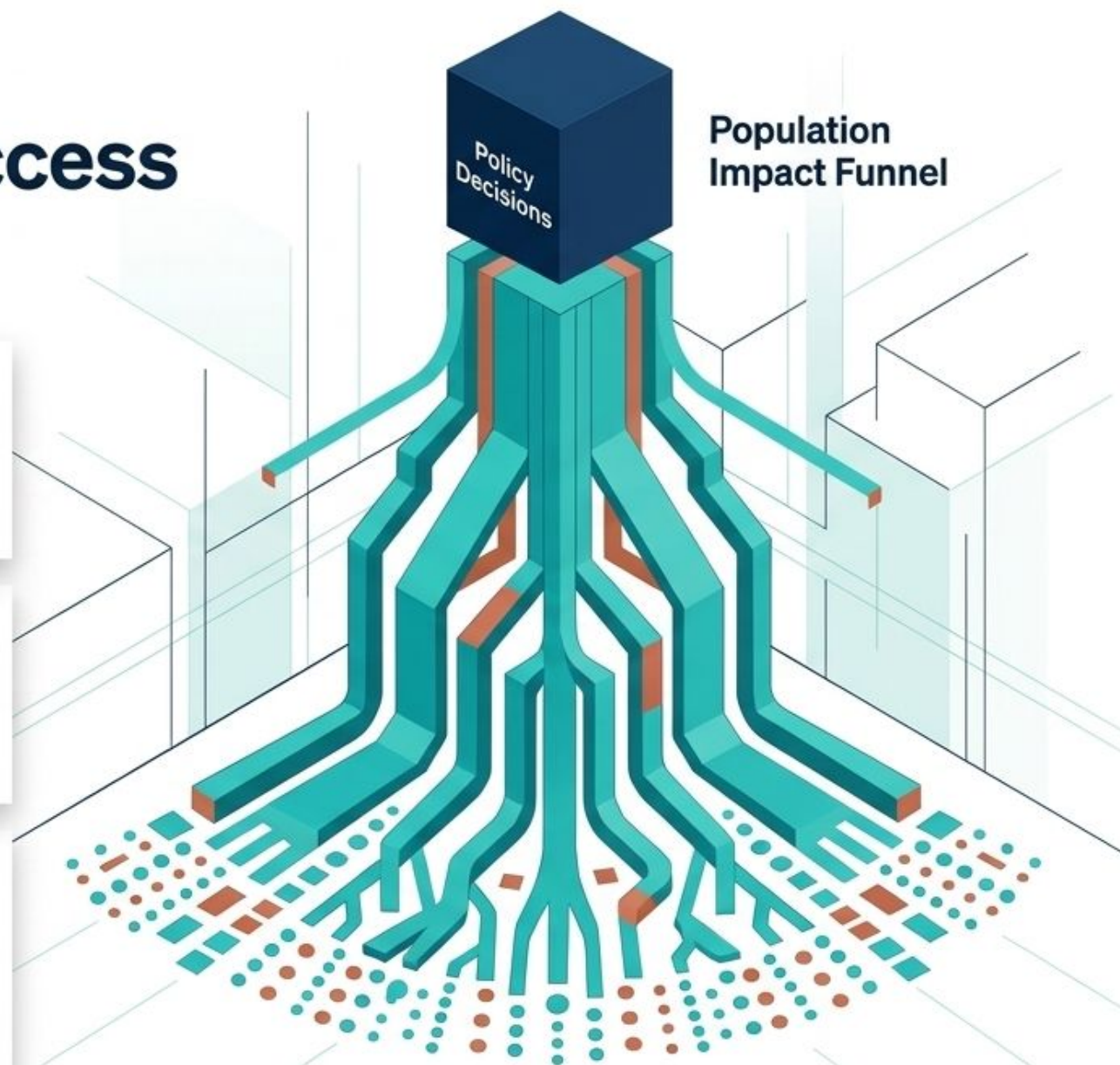
Long-term pharmacotherapy is essential to preventing disease progression at the population level.

Shift the Paradigm.

Obesity medications must be classified and implemented simultaneously with lifestyle, never as a mere adjunct.

Prioritize Access and Equity.

Policies must ensure advances benefit all populations, particularly those disproportionately affected by obesity and related complications.



THE MESSAGE TO REMEMBER!

