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OBESITY THE WEIGHT OF THE EPIDEMIC

DAVID M. H. CHASCSA, MD

- Assistant Professor of Medicine

Mayo Clinic Alix School of Medicine

- Consultant

Divisions of Gastroenterology & Hepatology and Transplant Center

- Co-Founder Mayo Clinic Arizona Metabolic Hepatology Clinic
- Diplomate American Board Obesity Medicine
- Member American Association for Study of Liver Diseases

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

All relevant financial relationships have been mitigated.

LEARNING OBJECTIVES

1. Demonstrate how obesity impacts the healthcare system
2. Identify how obesity affects different organ systems
3. Demonstrate understanding of the need for individualized treatment of obesity

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DEFINING OBESITY

DEFINING OBESITY

- Obesity is a chronic, relapsing, multifactorial disease characterized by abnormal or excessive adipose tissue accumulation that may impair health and significantly increase disease risks. Obesity is diagnosed in adults when body mass index (BMI) is ≥30 kg/m².

Obesity Class	BMI (kg/m²)	Asian BMI (kg/m²)
Overweight	25-29.9	23.0–27.4
1	30–34.9	27.5–32.4
2	35–39.9	32.5–37.4
3	≥40	≥37.5

Acosta et al. AGA 2017 doi:10.1016/j.cgh.2016.10.023
Obesity 2013 doi:10.1002/oby.20821
Mehta Circulation 2023 doi:10.1161/CIR.0000000000001139

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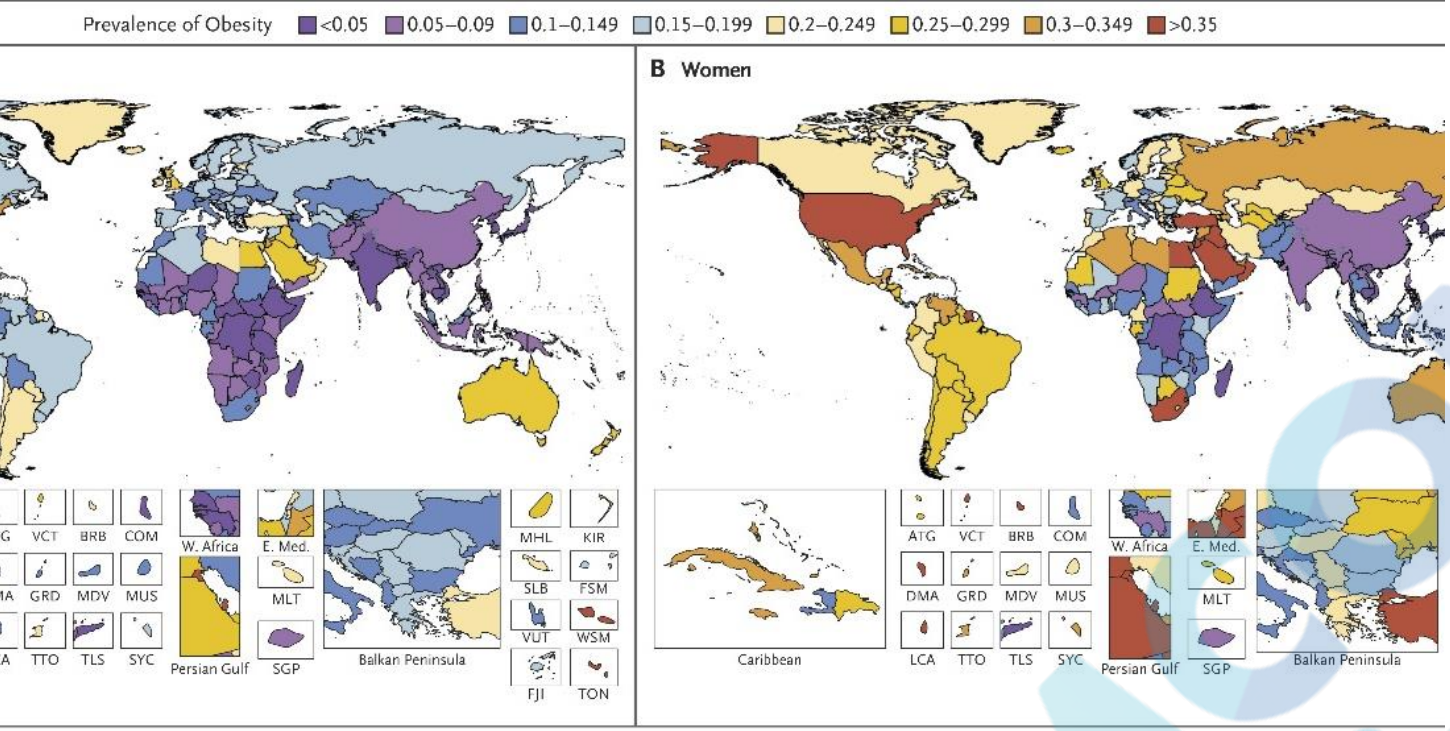
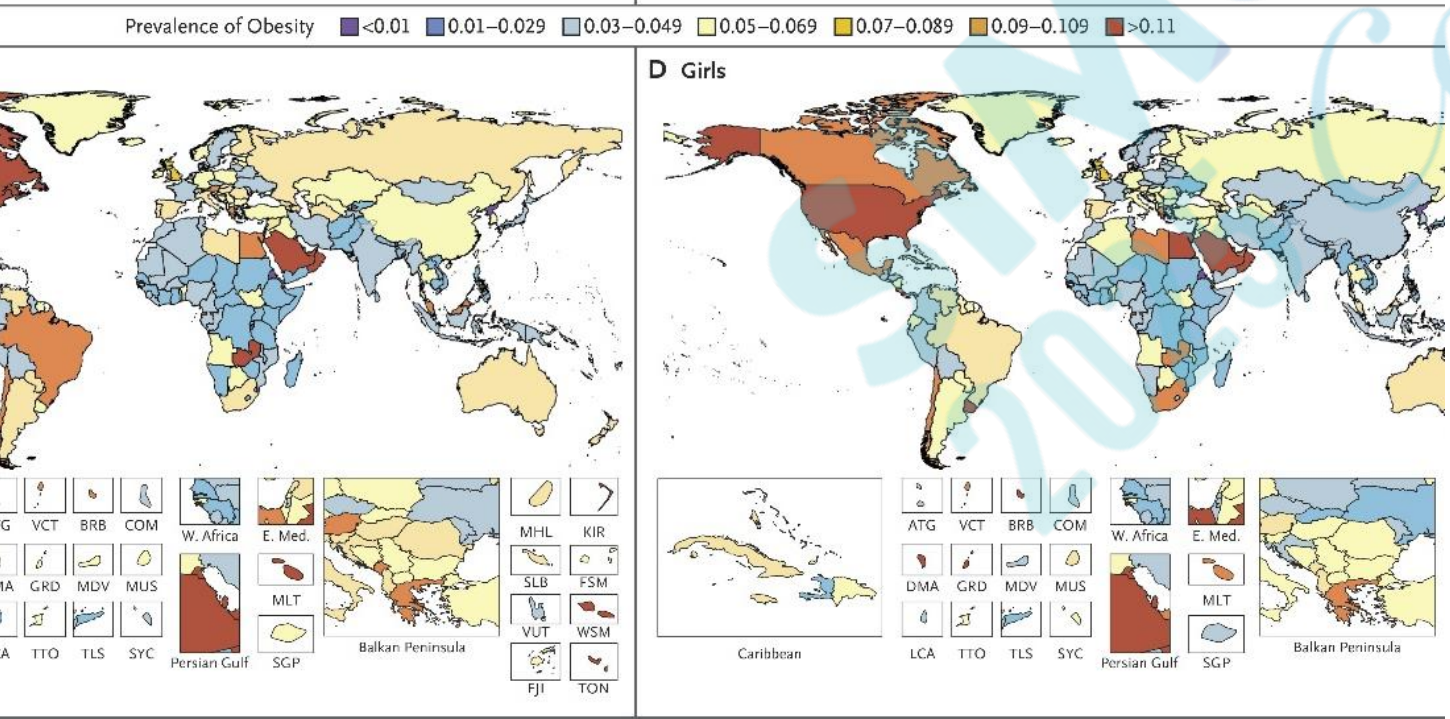
DEMONSTRATE HOW OBESITY IMPACTS HEALTHCARE

OBJECTIVE 1





GLOBAL BURDEN OF DISEASE

- **650,000,000 affected by obesity worldwide**
- **Depending on BMI cutoff obesity prevalence in Colombo is 15.8-31.2%**
- **0.7-2.8% of global healthcare expenditures; 2.42% country's GDP**
- **Each 5kg/m^2 increase in BMI above 25 increases overall mortality by 30%**
- **BMI > 40 reduces life expectancy by up to 10 years**

Afshin NEJM 2017 doi:10.1056/NEJMoa1614362
Somasundaram J Diabetes Res. 2019; doi:10.1155/2019/2046428
Carlsson NEJM 2023 doi: 10.1056/NEJMoa2002449
Nagi Int J Ob 2024 doi: 10.1038/s41366-023-01398-y

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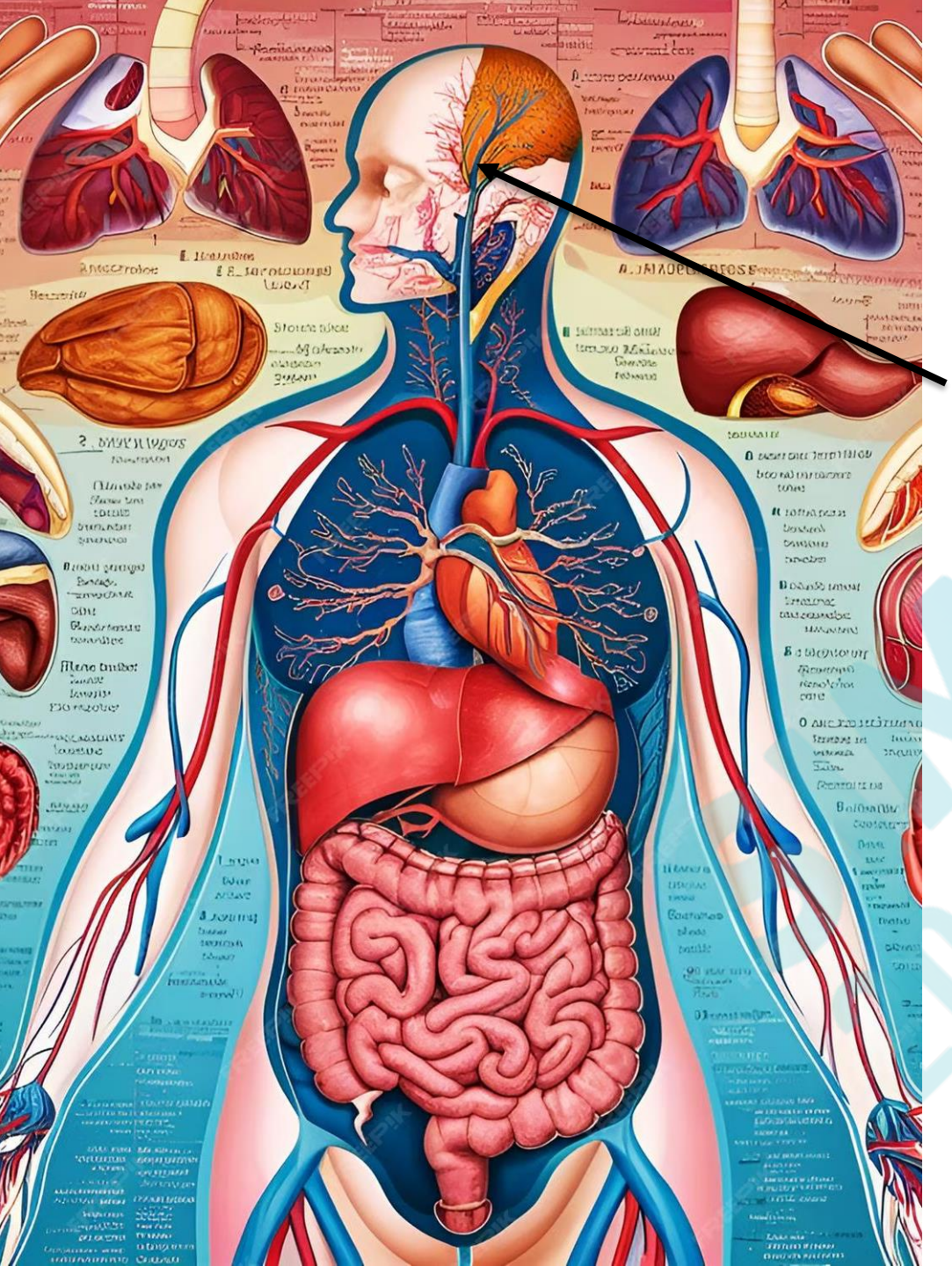
IDENTIFY THE IMPACT OF OBESITY ON DIFFERENT ORGAN SYSTEMS

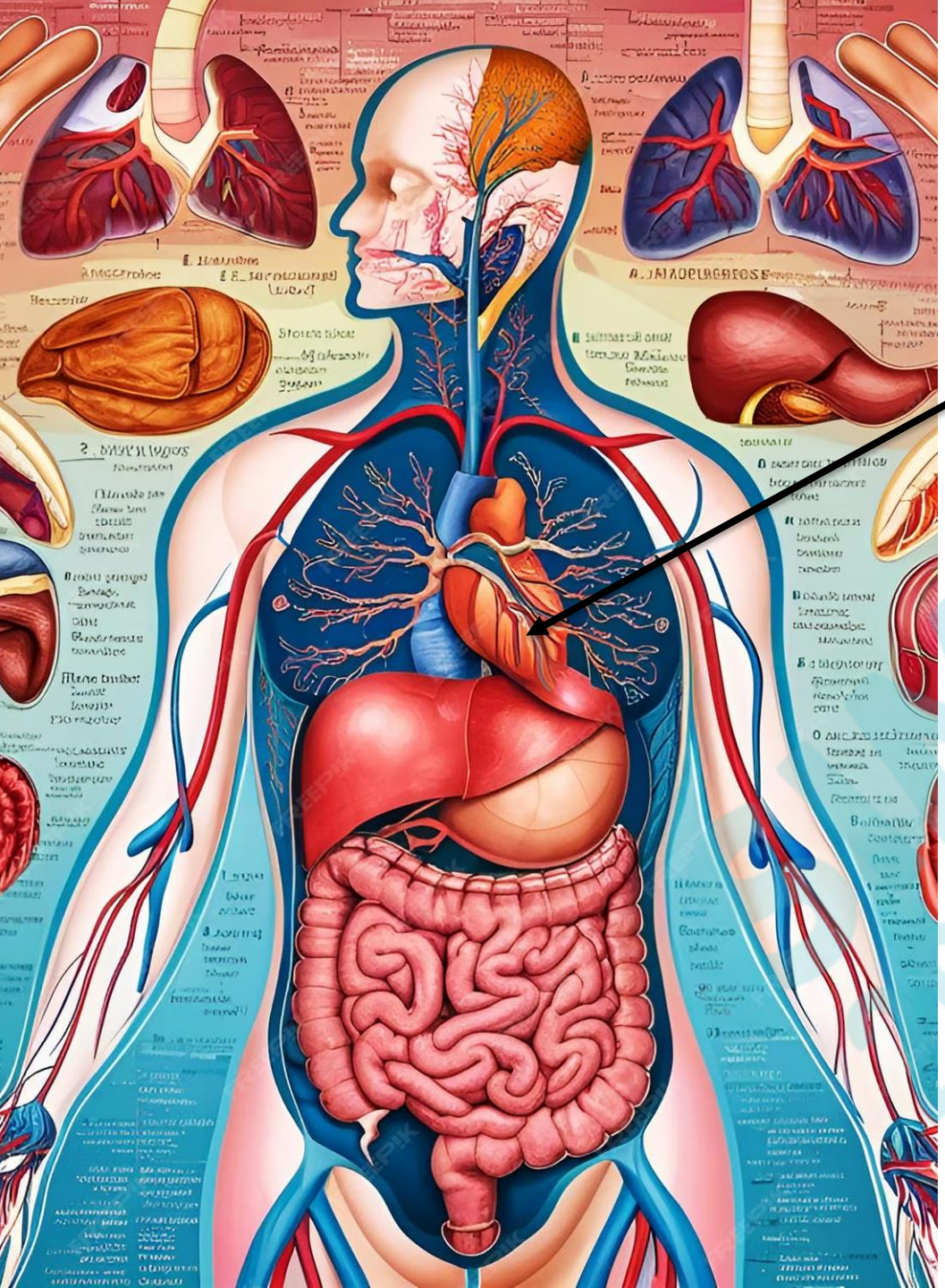
OBJECTIVE 2



NEUROLOGIC

- Neuroinflammation from excess adipose tissue
- Structural brain changes including reduced gray and white matter
- Cognitive impairment and increased risk of neurodegenerative disease

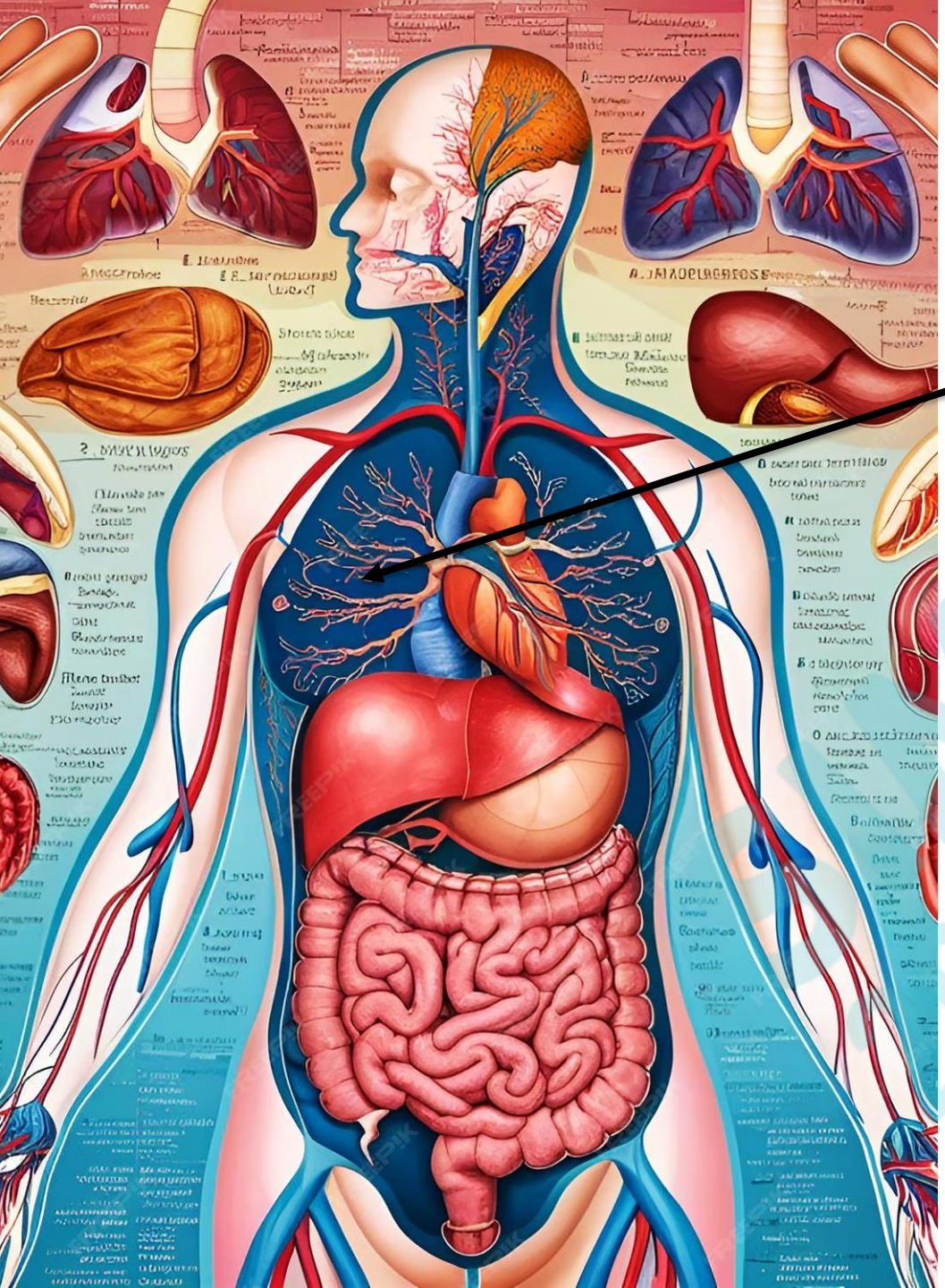
Olsthoorn *Front Neurosci*. 2021 doi:10.3389/fnins.2021.761456



CARDIOVASCULAR

- Lipid accumulation and vascular inflammation lead to atherosclerosis and coronary artery disease
- Venous thromboembolism
- Valvular heart disease
- Heart failure with preserved ejection fraction

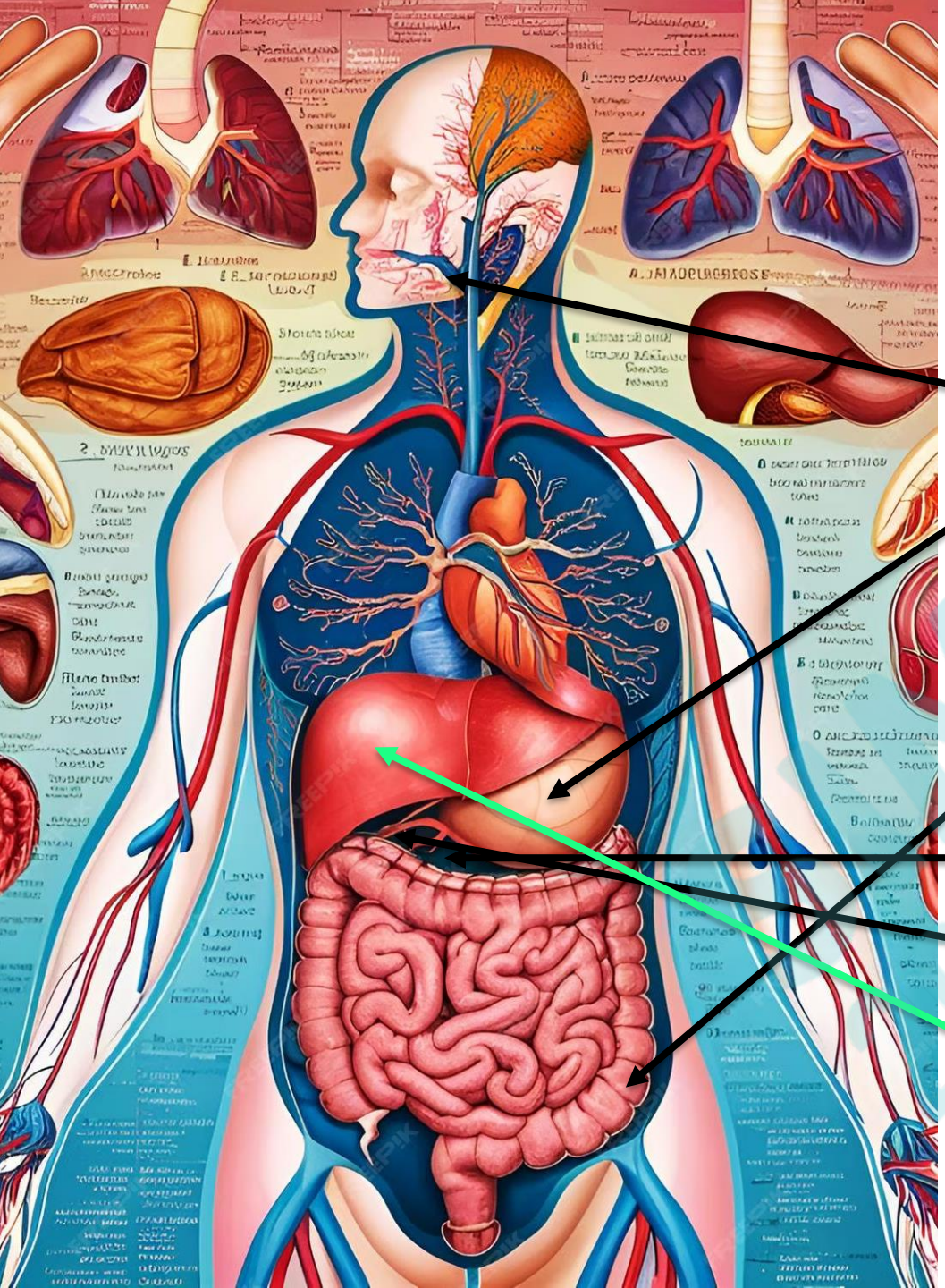
Powell-Wiley Circulation 2021 doi:10.1161/CIR.0000000000000973



PULMONARY

- Excess adipose tissue restricts diaphragmatic movement and increases pleural pressure leading to reduced lung volumes, ventilation perfusion mismatch and hypoxemia
- Obesity hypoventilation syndrome results in hypercapnia
- Obstructive sleep apnea
- Pulmonary hypertension

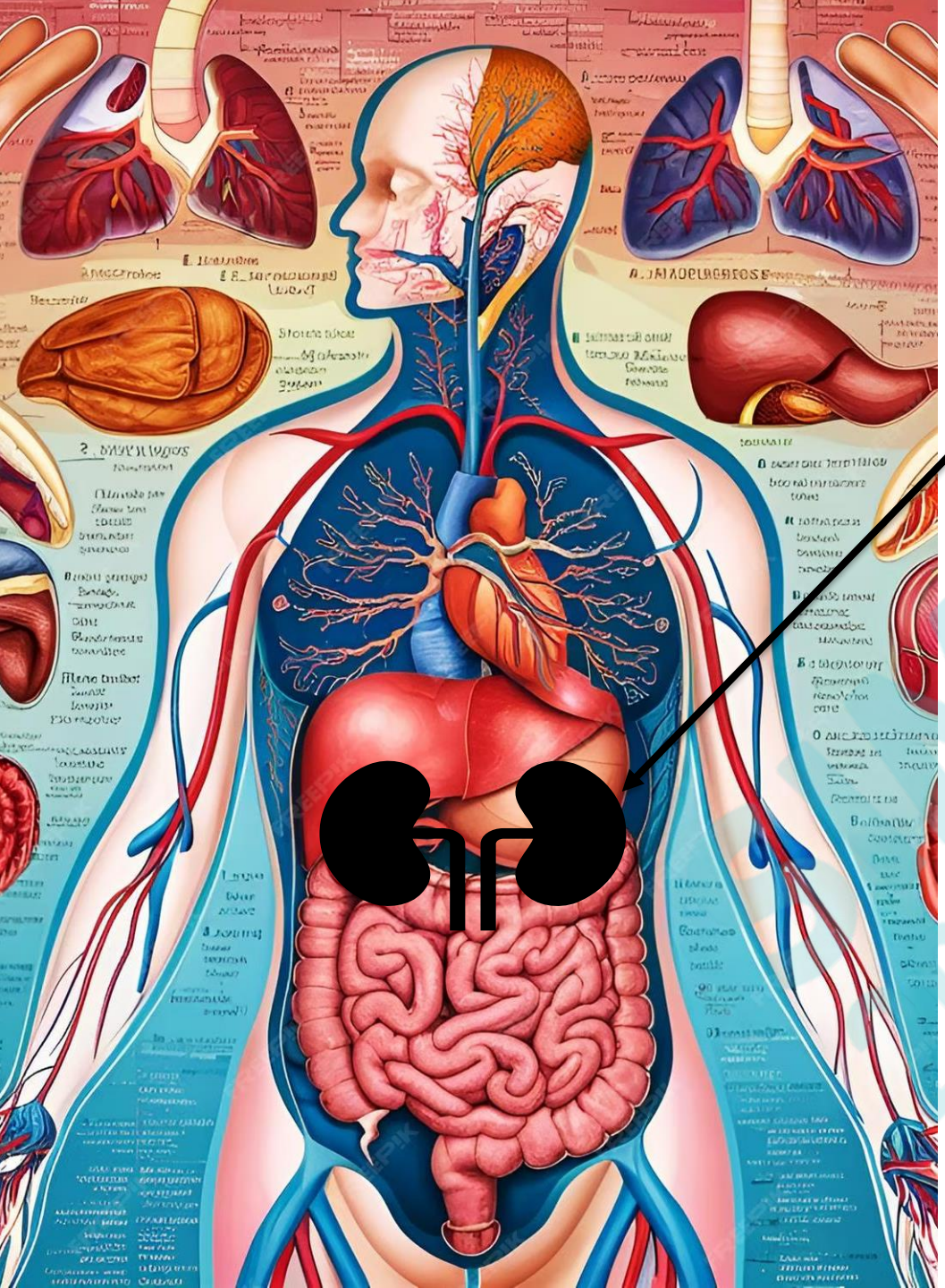
Rabec Euro Rsp doi:10.1183/16000617.0190-2024



GASTROINTESTINAL

- GERD
- Abdominal pain, visceral hypersensitivity, erosive gastritis
- Chronic diarrhea, diverticular disease
- Colorectal adenomas and cancer
- Pancreatitis
- Cholelithiasis
- Metabolic dysfunction associated steatotic liver disease (full discussion at MasterClass)

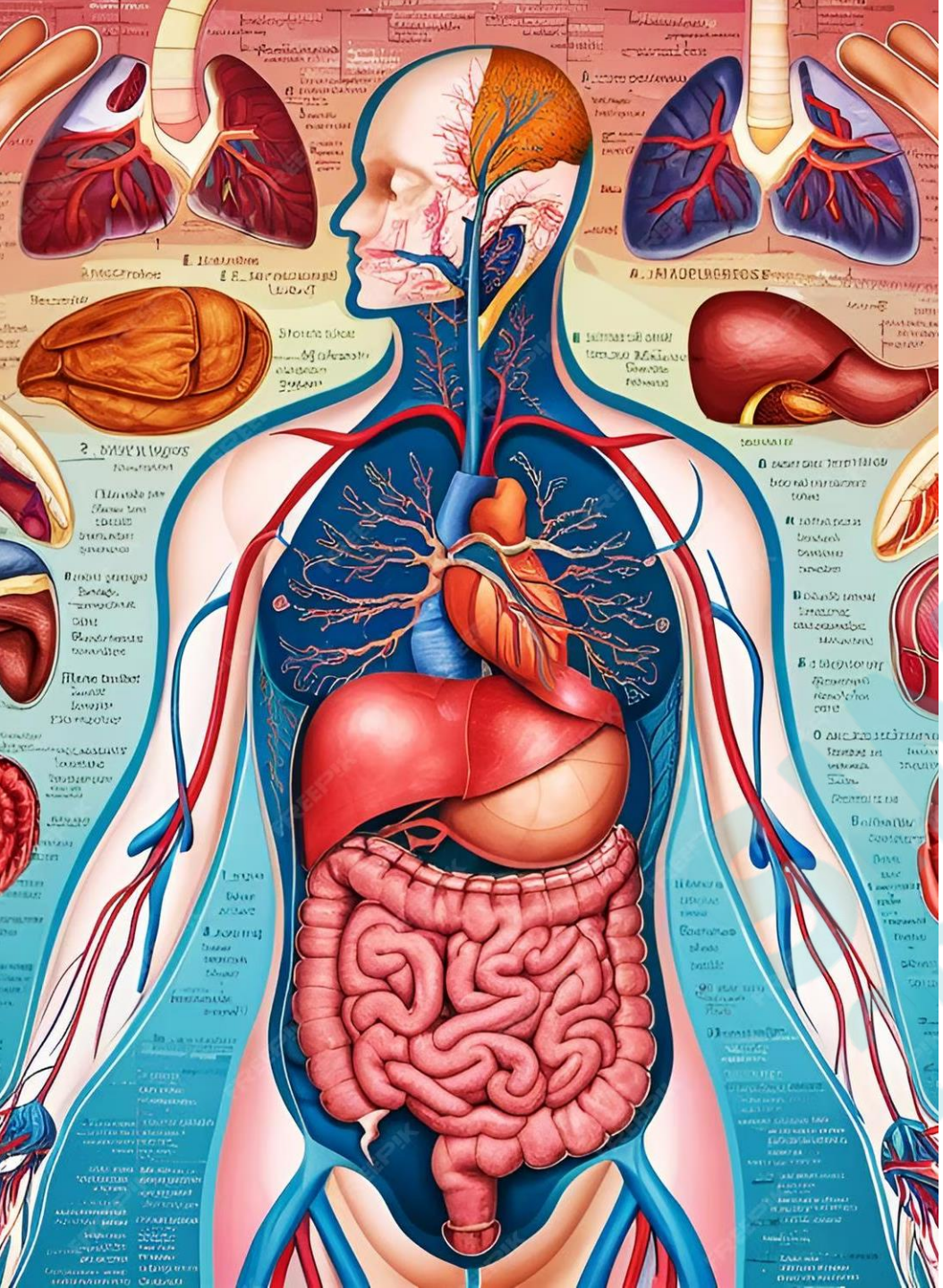
Camilleri Gastroenterology 2017 doi:10.1053/j.gastro.2016.12.052



GENITOURINARY

- With each 5-unit BMI increase, the risk of urinary incontinence rises by 20–70% in women
- Overactive bladder, nocturia
- Pelvic floor disorders, including prolapse
- Glomerulonephropathy and CKD
- Nephrolithiasis
- BPH
- Sexual dysfunction

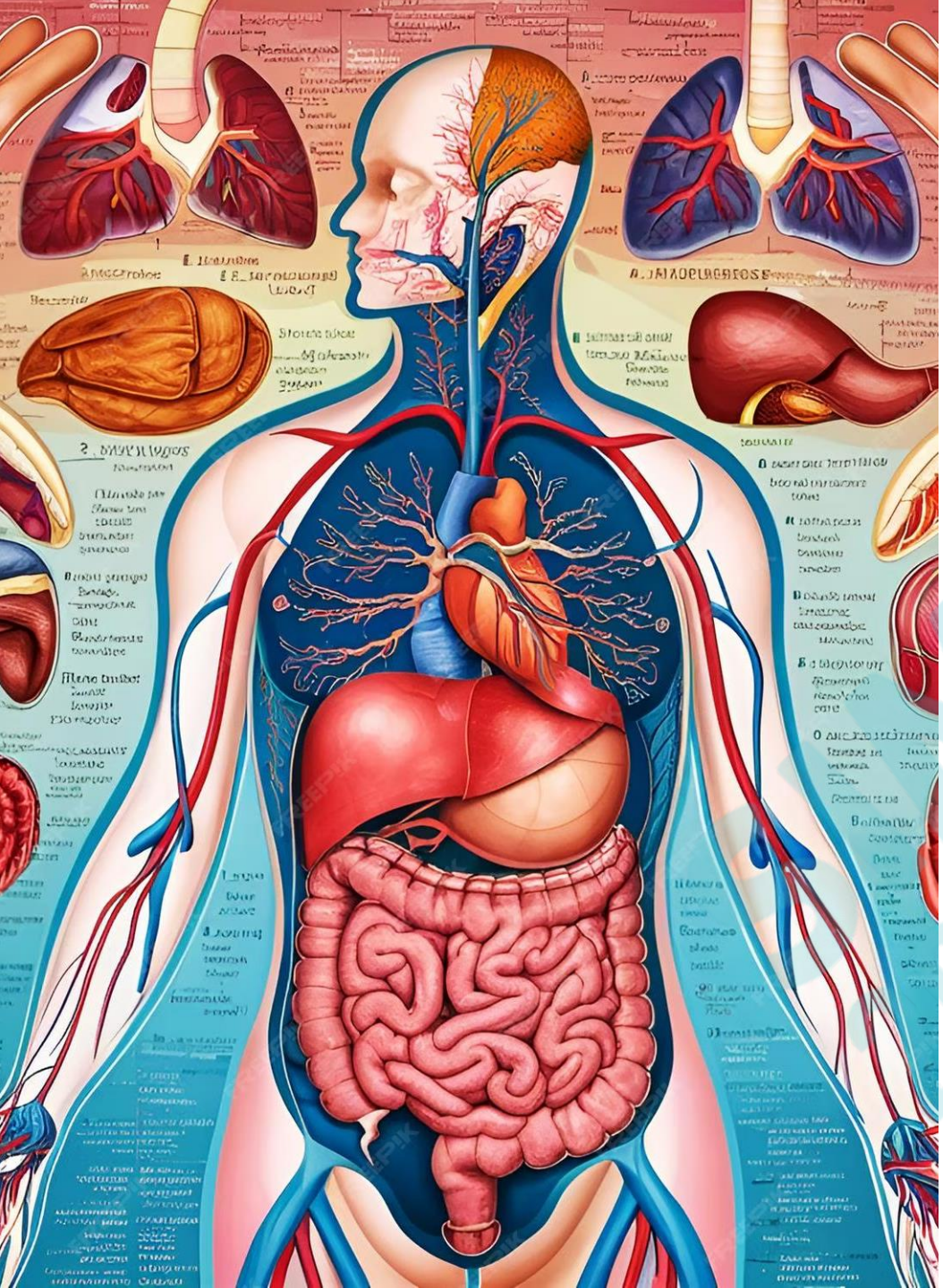
Pomian Medical Science Monitor 2016 doi:10.12659/msm.896331
Natarajan The Jur of Uro 2009 doi:10.1016/j.juro.2009.01.107



ENDOCRINOLOGICAL

- Insulin resistance/diabetes
- Thyroid dysfunction
- Gonadal dysfunction
  - Low testosterone (m)
  - Hyperandrogenism (w)
- PCOS
- Growth hormone deficiency

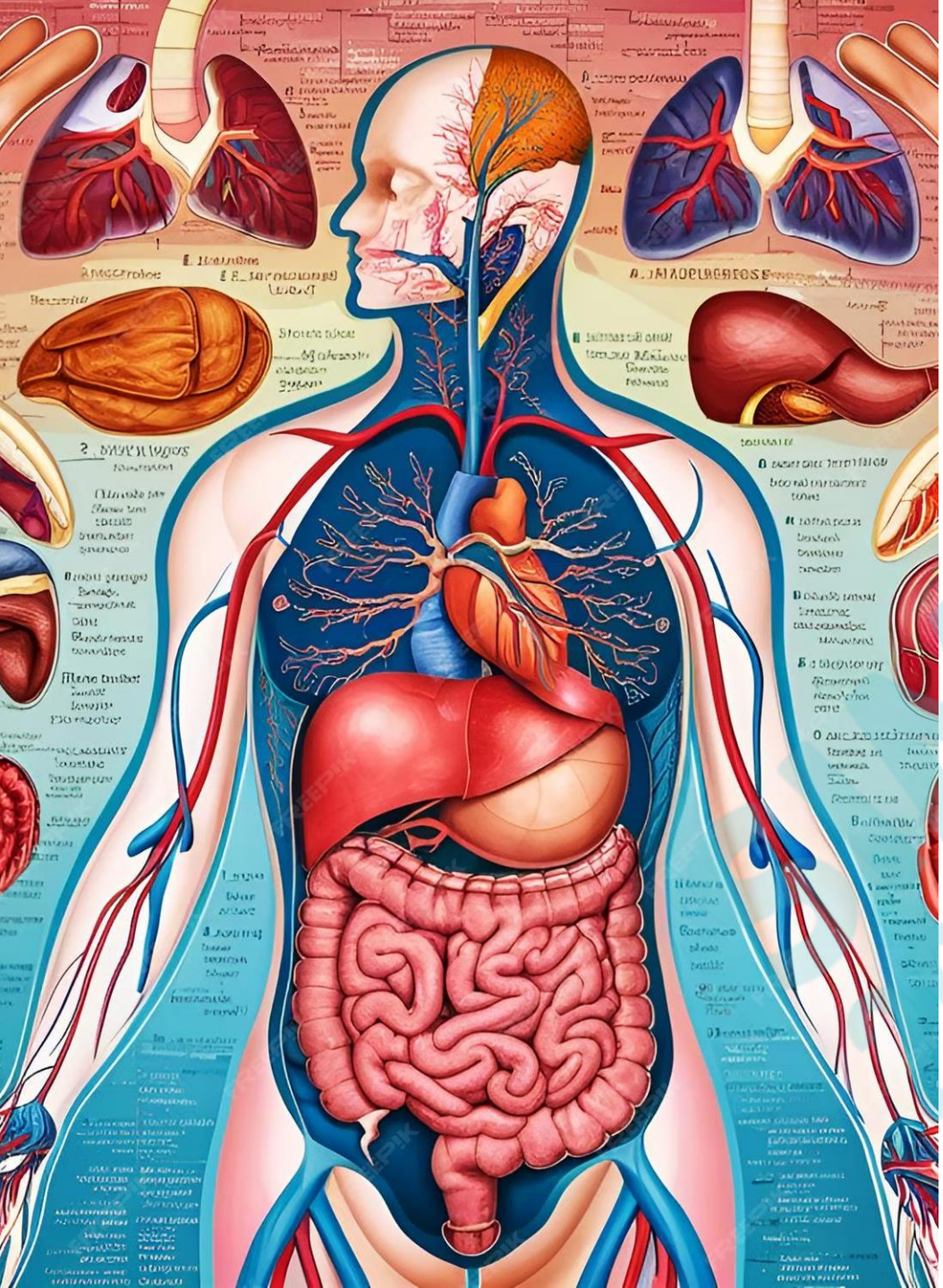
Van Hulsteijn Euo Jrnl Endo 2020 doi:10.1530/EJE-19-0666



MUSCULOSKELETAL

- Osteoarthritis is the most common complication of obesity affecting 91% of patients
- Impaired mobility and independence

Kloppenburg Lancet 2025 doi:10.1016/S0140-6736(24)02322-5



DERMATOLOGIC

- Skin tags
- Acanthosis nigricans (hyperpigmentation)
- Intertrigo
- Psoriasis
- Hidradenitis suppurativa
- Poor wound healing
- Lymphedema
- Lipedema

Hirt Jrnl AA Derm 2019 doi:10.1016/j.jaad.2018.12.070

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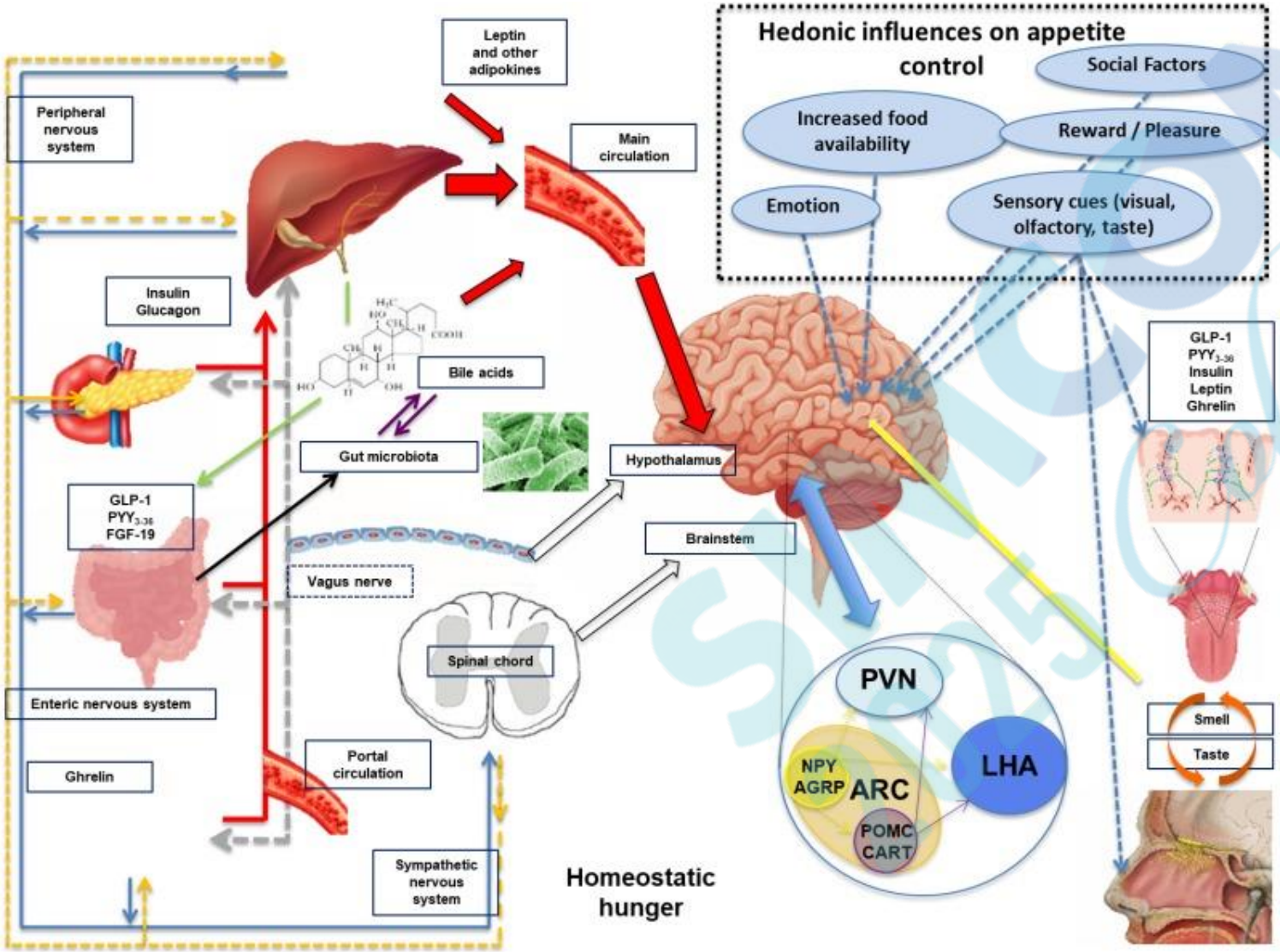
TREATMENT

OBESITY. *n.*
Chronic, relapsing, physiologic resistance

Objective 3

Image Freesvg.org

WHY IS OBESITY SO HARD TO TREAT



- Increased appetite
- Decreased energy expenditure
- Defense of a higher set point

- Multiple mechanisms:
  - Hedonic
  - Satiation
  - Satiety
  - Reduce energy expenditure

Kompaniyets JAMA Netw Open. 2023 doi: 10.1001/jamanetworkopen.2023.27358

TREATMENT TO INDUCE A CALORIC DEFICIT

- Calorie restriction is more important than dietary composition
  - Low energy diet 800-1800kcal/d or energy deficit 500-750 kcal/d
    - Patients underestimate caloric intake by 30-50%
    - Patient drop out about 20%
  - Portion controlled diets work but are expensive
  - Equivalent weight loss at one year with low fat vs low carb
    - Evidence supports more weight loss with Mediterranean diet
  - Time restricted eating may benefit some patients
- Exercise?

Chao J Clin Invest. 2021doi: 10.1172/JCI140065

EFFICACY OF TREATMENT?

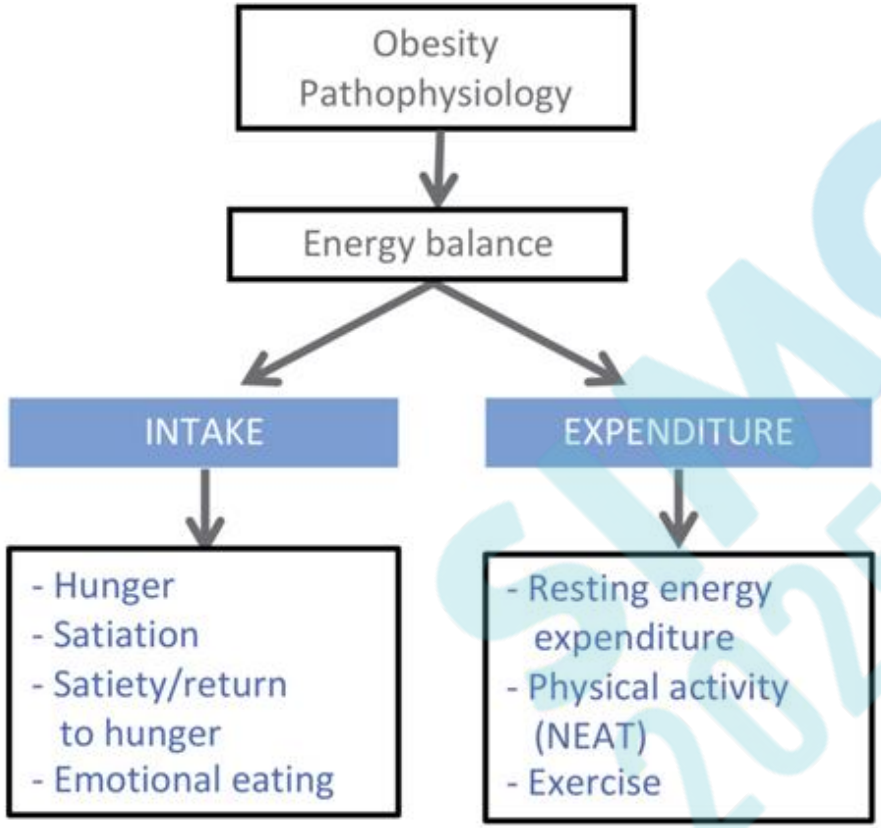
- 1 in 10 patients achieve ≥5% weight loss
- 1 in 1667 patients with Class III obesity achieve a healthy weight based on BMI

AGENTS TO TREAT OBESITY

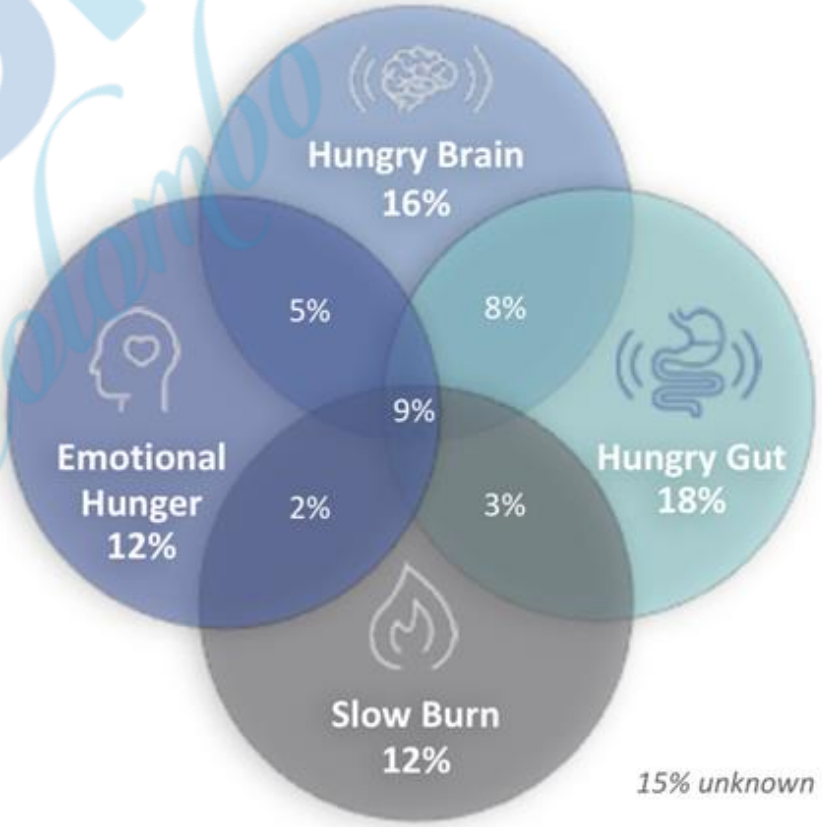
Agent	Mechanism of action	Total body weight loss (%)
Liraglutide	GLP-1 agonist mimics gut hormone and slows digestion and suppresses appetite	5-10
Semaglutide	GLP-1 agonist	15
Tirzepatide	Dual GIP/GLP-1 agonist enhances insulin secretion and reduces appetite	20
Phentermine	Sympathomimetic stimulates CNS to reduce hunger	5-10
Phentermine/topiramate	Reduces hunger and increases satiety	10-12
Naltrexone/Bupropion	Targets reward system to reduce appetite	5-7
Orlistat	Lipase inhibitor; fat malabsorption	5-7
Setmelanotide	MC4 receptor agonist, regulates hunger in genetic cause of obesity	Varied

FOUR OBESITY PHENOTYPES

A

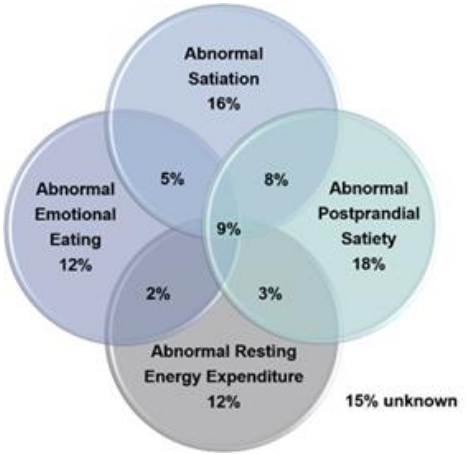


B



Acosta Obesity, 2021 DOI: 10.1002/oby.23120

PRECISION PHARMACOTHERAPY

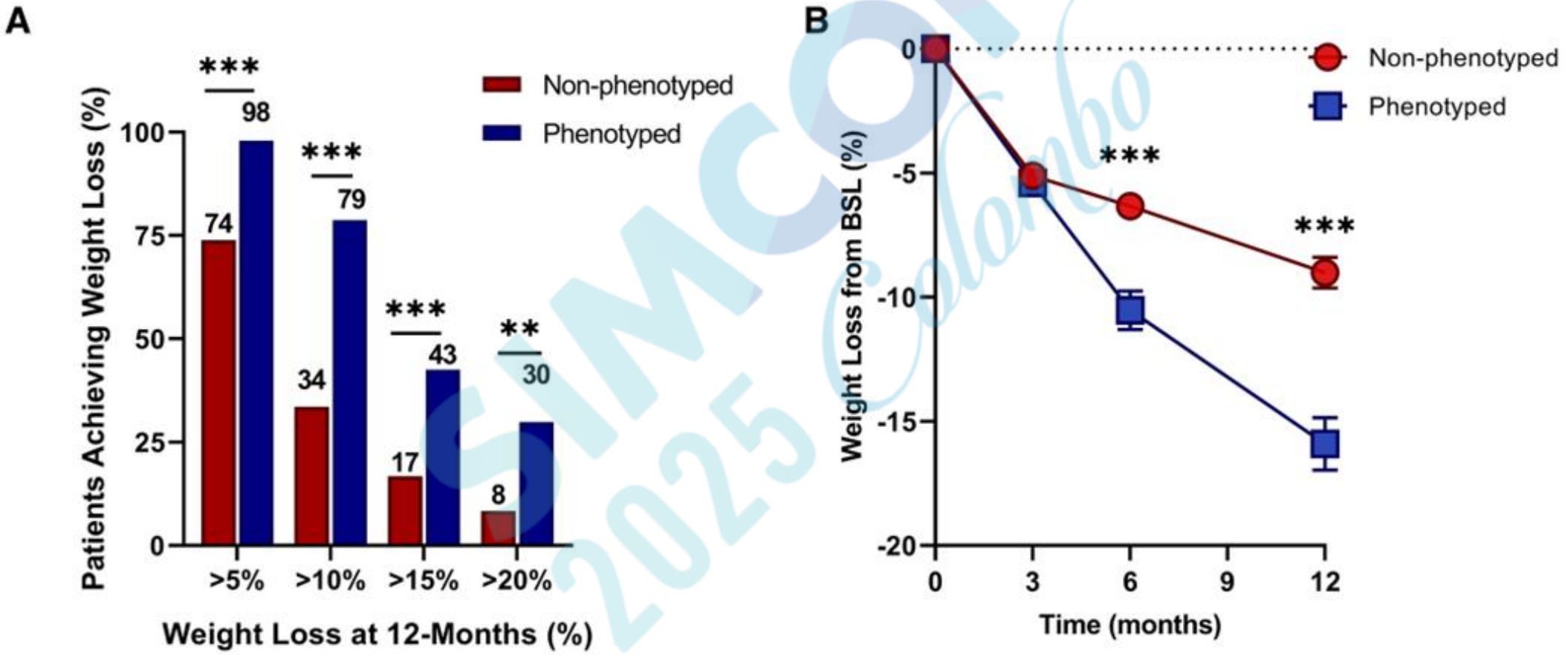


Eval	Results	Diagnosis	Intervention
Nutrient Drink Test	Higher calories to reach fullness	Abnormal Satiation (hungry brain)	Phentermine-Topiramate ER
Questionnaire after *ad libitum* meal + Gastric Emptying	Accelerated Gastric Emptying + Higher fasting volumes	Abnormal Satiety (hungry gut)	Liraglutide Semaglutide Tirzepatide
Questionnaires HADS and TFQ-21	Higher anxiety and depression scores	Abnormal Hedonic Eating	Naltrexone-Bupropion SR
Indirect Calorimetry + DEXA	Decreased energy expenditure	Abnormal Resting Energy Expenditure	Exercise

Phenotype	Definition of abnormal (25th or 75th percentile of normal)
Abnormal Satiation	>894 kcal (f) or > 1376 kcal (m) buffet meal; OR NTD women: volume to fullness (VTF) >750 ml (kcal), Maximal Tolerated Volume (MTV) >1422 ml (kcal). Men: VTF >1125 ml (kcal), MTV >1951 ml (kcal)
Abnormal Satiety	Gastric emptying <101 mins (f) or <86 mins (m); OR VAS scale – Fullness 120 min postprandial <42mm(f) <49(m) using a nutrient drink test
Hedonic Eating	HADS score ≥7 points
Low Predicted Energy Expenditure	<96% predicted REE (f) or <94% predicted REE (m)

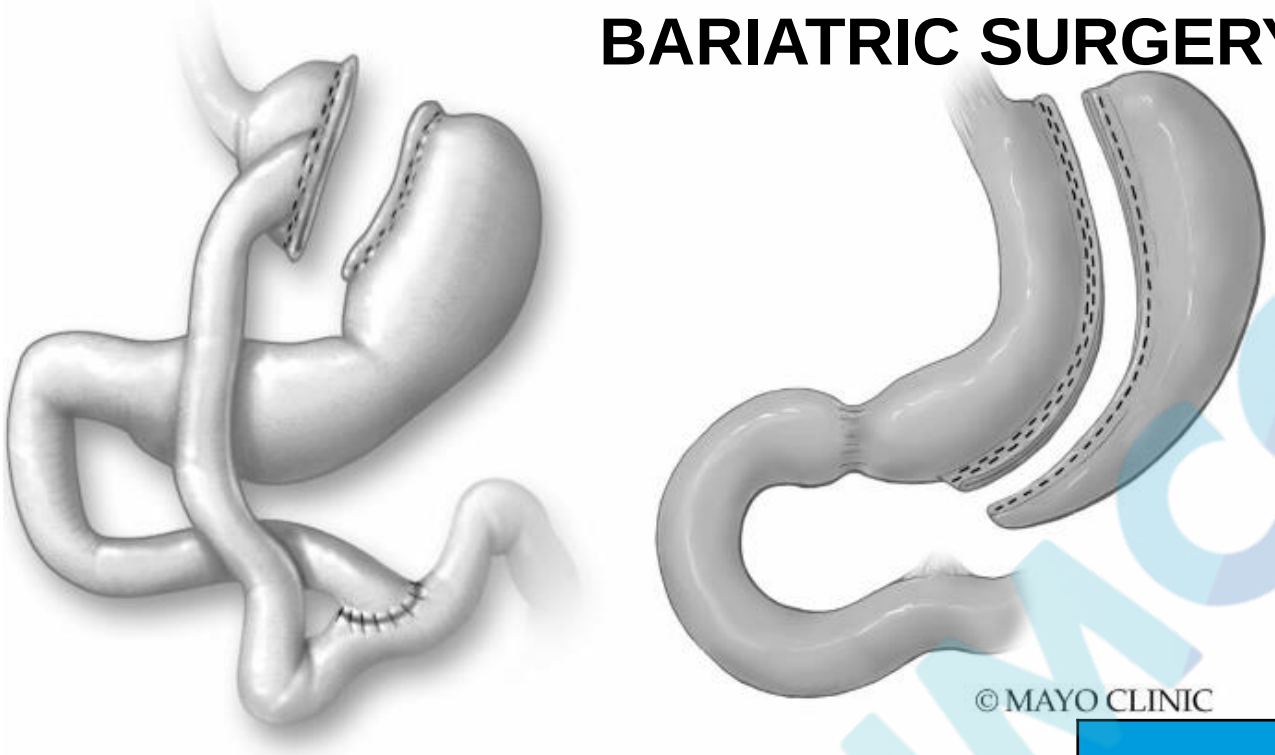
Acosta Gastroenterology 2015 10.1053/j.gastro.2014.11.020

PHENOTYPE DIRECTED THERAPY IS MORE EFFECTIVE



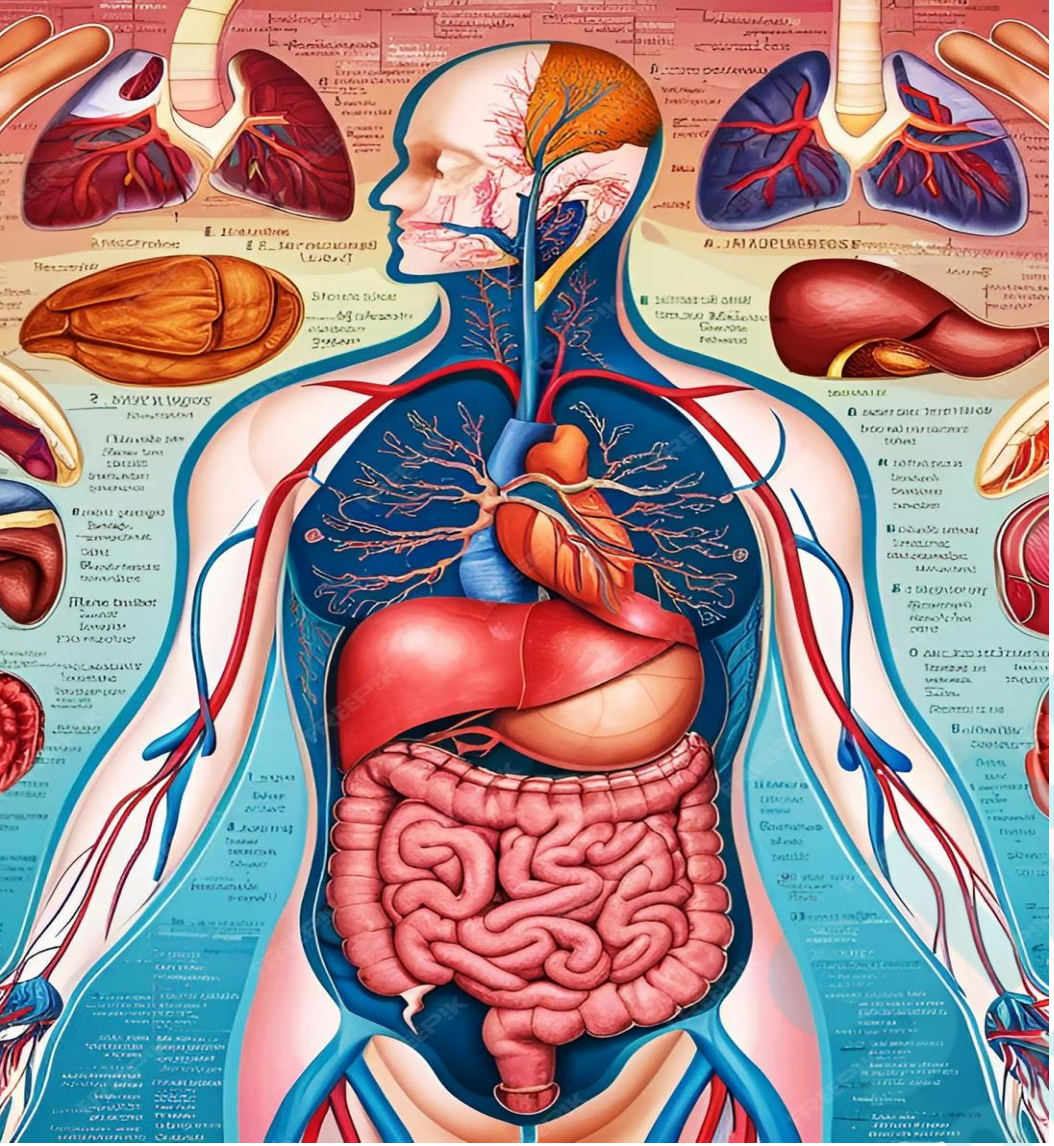
Acosta Obesity, 2021 DOI: 10.1002/oby.23120

BARIATRIC SURGERY AND ENDOSCOPY



- Weight loss may be as high as 30%
- Resolves MASH and comorbidities
  - 80% at 1-5 years

Procedure	Total weight loss (%)
Roux-en-Y	**31**
Sleeve gastrectomy	**25**
Endoscopic • **Intragastric balloon** • **Sleeve**	**10-18**



WEIGHT LOSS IMPROVES HEALTH AND WELLBEING

- Improves brain age
- Reduces major adverse cardiovascular events
- Increases lung function; decreases symptoms
- Dose dependent reductions in GI symptoms and disease (e.g., GERD, MASLD)
- Resolution of urinary incontinence, LUTS, slows CKD
- Improved glucose metabolism, resolution of PCOS, hypogonadism
  - Thyroid dysfunction may persist
- Dose dependent improvement in mobility, may improve pain scores
- Beneficial impact on psoriasis, acanthosis

Zeighami NeuroImage. 2022 doi:10.1016/j.neuroimage.2022.119415
Chen International Journal of Obesity 2025 doi:10.1038/s41366-025-01860-z
Held PloS One 2014 doi:10.1371/journal.pone.0107480
Tahrani J. Obesity 2022 doi:10.1002/oby.23371
Marcelissen Neurourology and Urodynamics. 2019 doi:10.1002/nau.24072
Fanni Diabetes, Obesity & Metabolism. 2025. doi:10.1111/dom.16526
Ford JAMA Dermatology. 2018;154(8):934-950. doi:10.1001/jamadermatol.2018.1412

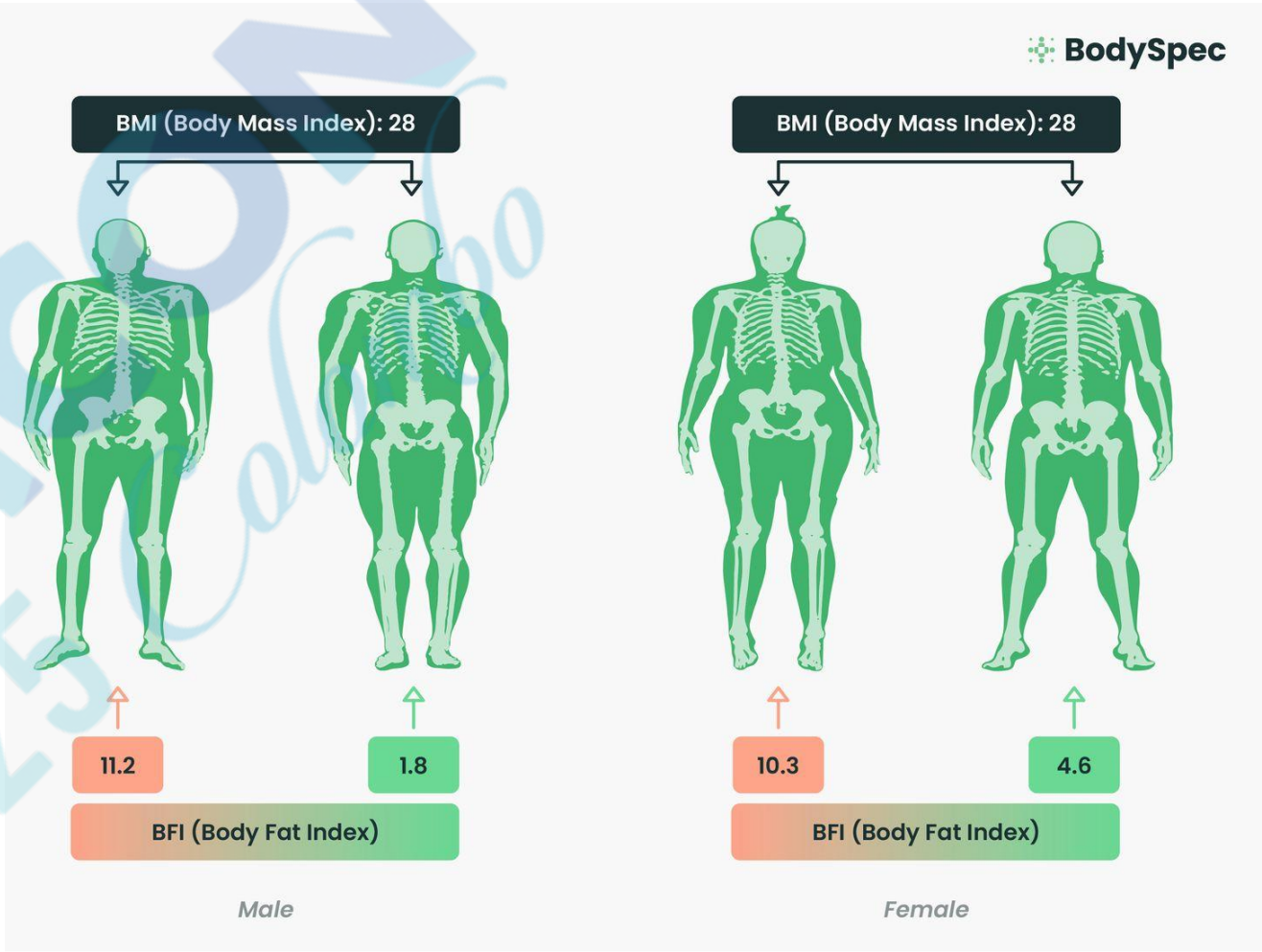
WHAT IF WE CAN'T ACHIEVE A HEALTHY BMI?

- J-shaped curve with BMI and health outcomes
- Measurements superior to BMI to predict outcomes:
  - Fat Mass Index (FMI)
  - Waist to Hip ratio (WHR)

What your Waist-to-Hip Ratio Means

WOMEN	HEALTH RISK	BODY SHAPE
0.80 or below	Low	Pear
0.81 to 0.85	Moderate	Avocado
0.85+	High	Apple

MEN	HEALTH RISK	BODY SHAPE
0.95 or below	Low	Pear
0.96 to 1.0	Moderate	Avocado
1.0+	High	Apple



Khan JAMANetworkOpen 2023 doi:10.1001/jamanetworkopen.2023.34836

PREVENTION IS KEY

- Population health system-based interventions:
  - Sweetened beverage taxes
  - Advertising restrictions
  - Focus on healthy nutrition at school
  - Focus on movement

SUMMARY

- Obesity is a chronic and relapsing disease which affects every organ system in the body.
- Weight loss is incredibly difficult to achieve and maintain, but can reverse the deleterious affects of obesity
- Precision pharmacologic therapy in addition to lifestyle modification has the best chance at successfully controlling obesity

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THANK YOU FOR YOUR ATTENTION

Rochester, Minnesota

Phoenix, Arizona

Jacksonville, Florida