How can the Excess Weight be Removed?

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Obesity is recognised as a disease and health issue

WOF

"The World Obesity Federation takes the position that **obesity is a chronic, relapsing, progressive disease process** and emphasizes the need for immediate action for prevention and control of this global epidemic"[1]

FDA

"Obesity is a chronic relapsing health risk defined by excess body fat"[3]

AMA

"American Medical Association recognizes obesity and overweight as a chronic medical condition and urgent public health problem…and work towards the recognition of obesity intervention as an essential medical service…"[2]

EMA

"Obesity is recognised as a chronic clinical condition and is considered to be the result of interactions of genetic, metabolic, environmental and behavioural factors, and is associated with increases in both morbidity and mortality"[6]

Bray *et al*. *Obes Rev* 2017;18:715–23; 2. AMA resolutions. June 2012. Available here; 3. Food and Drug Administration. Guidance for Industry Developing Products for Weight Management 2007 Available here; 4. Obesity Canada. Available here; 5. EASO: 2015 Milan Declaration: A Call to Action on Obesity. Available here; 6. EMA Draft Guideline on clinical evaluation of medicinal products used in weight control EMA/CHMP/311805/2014. Available here.

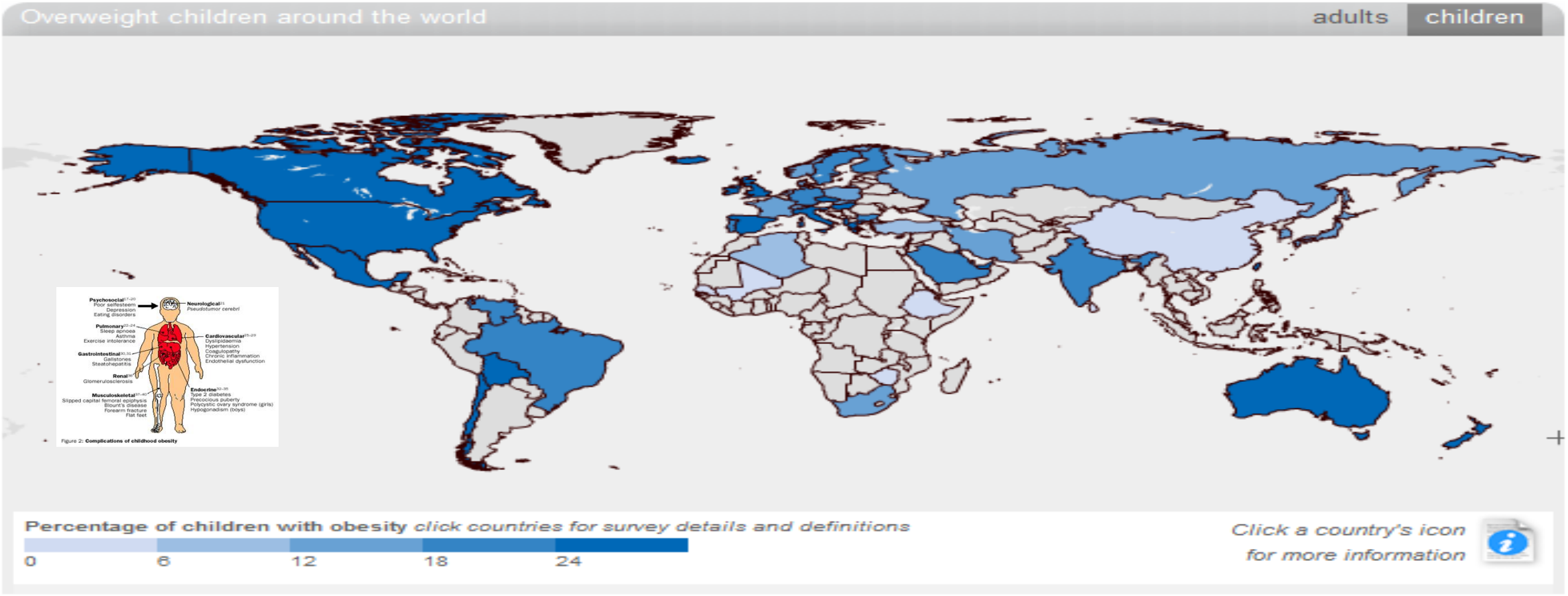
Nagoya Declaration 2015
- *Obesity is a "disease" !*

Obesity is a prevalent disease worldwide

In 2022, 2.5 billion adults are obese or overweight(43%). Among them, 0.89 billion are obesity(16%) .

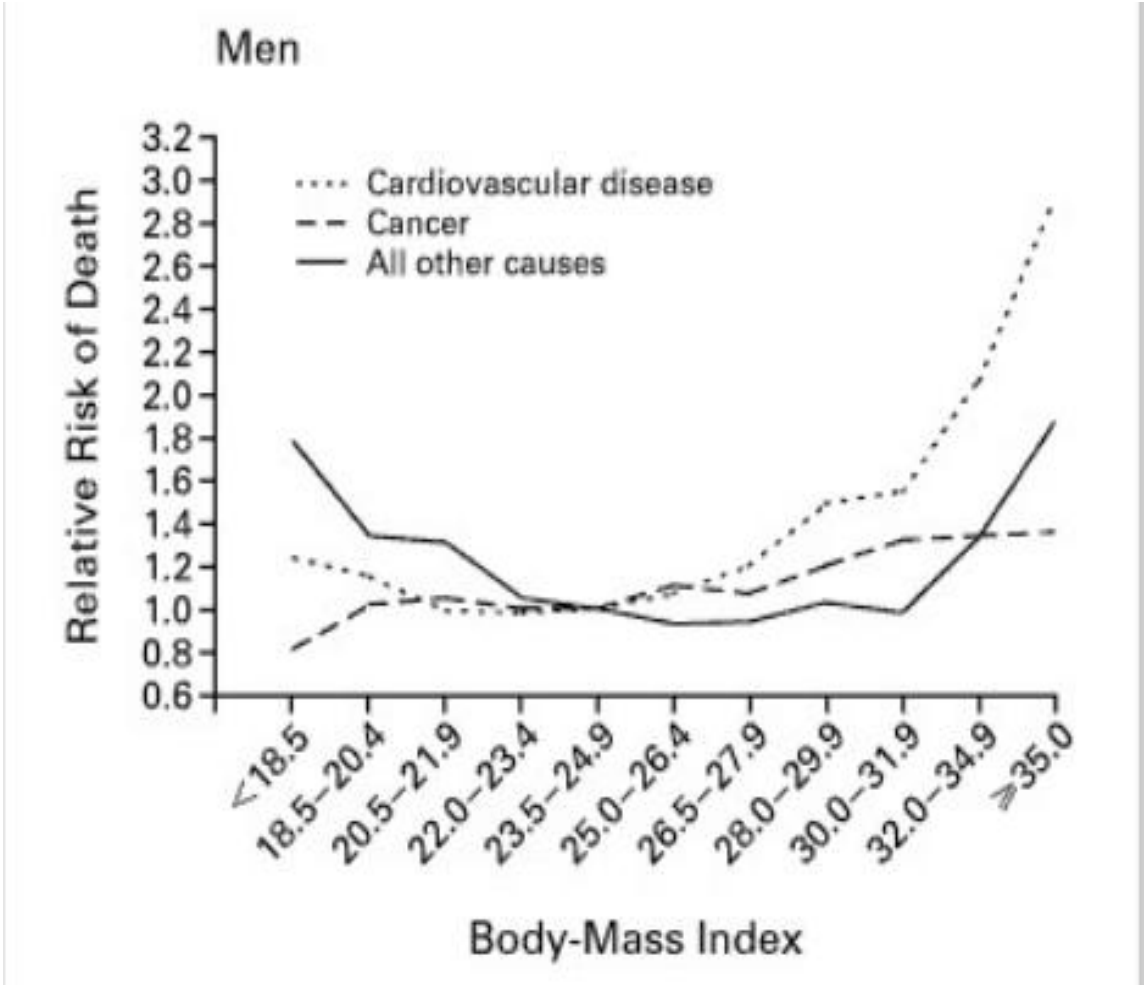
World map of obesity

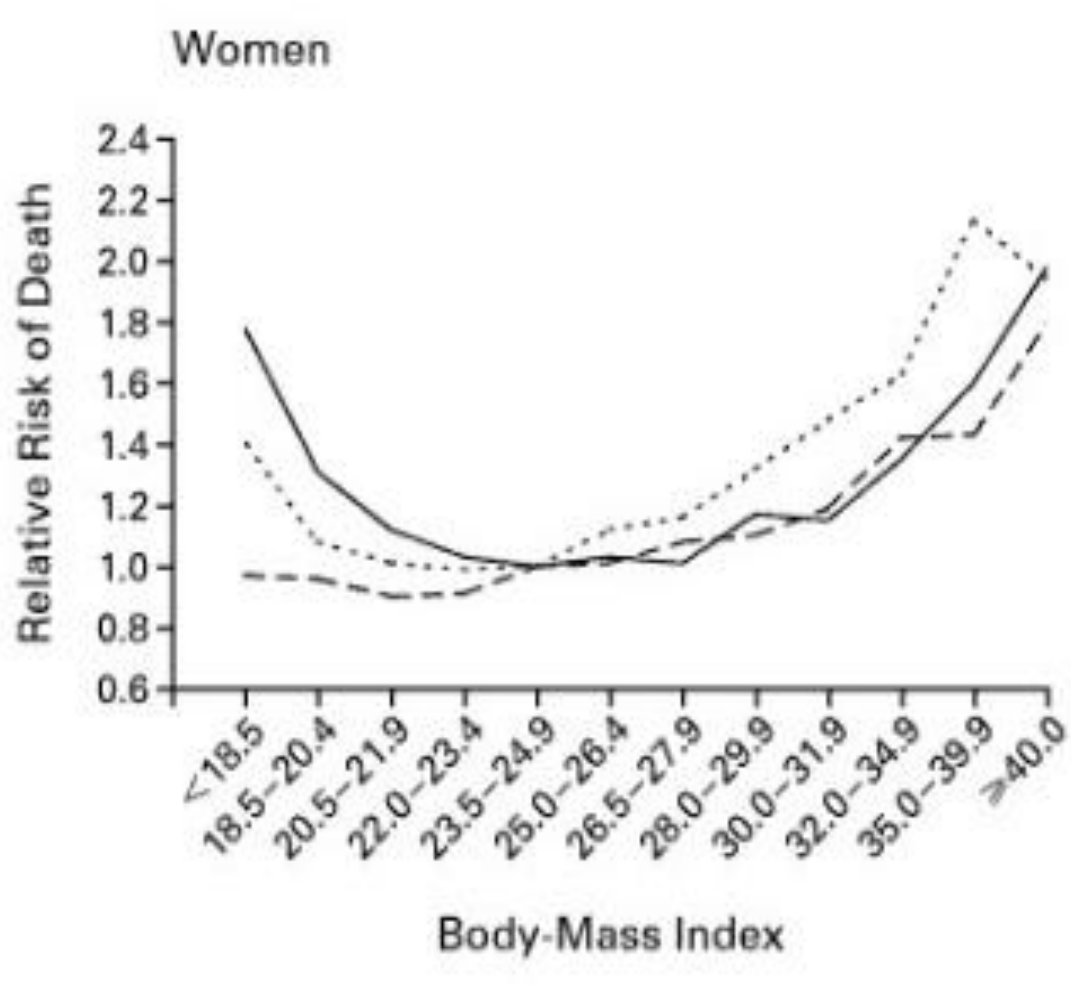
Explore our database of obesity prevalence worldwide. You can see detailed reports for any country for which we have data. Just click to zoom in. Then click the "info" icon to see a report. (Requires the "Flash" plugin to work).



Body-mass Index and Mortality in a Prospective Cohort of U.S. Adults

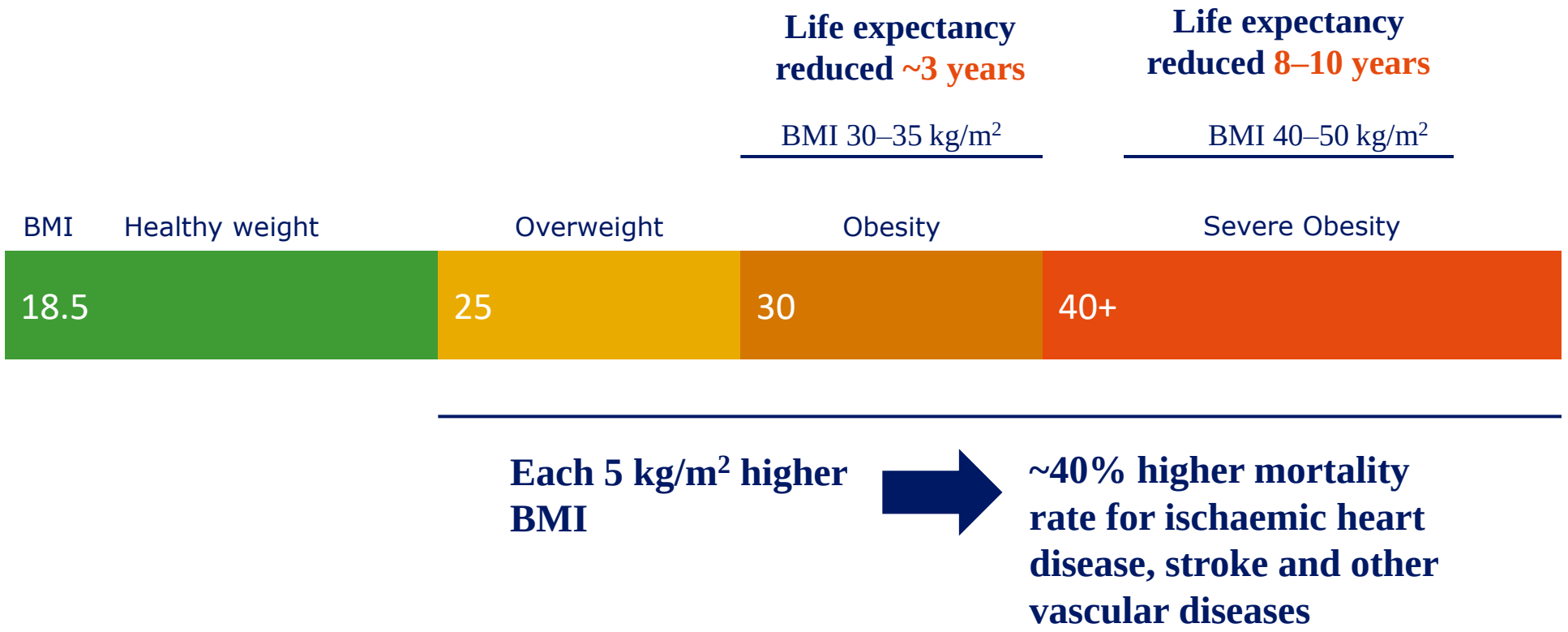
1+ million adults in the United States during 14 years of follow-up





N Engl J Med. 1999 Oct 7;341(15):1097-105.

Life expectancy decreases as BMI increases

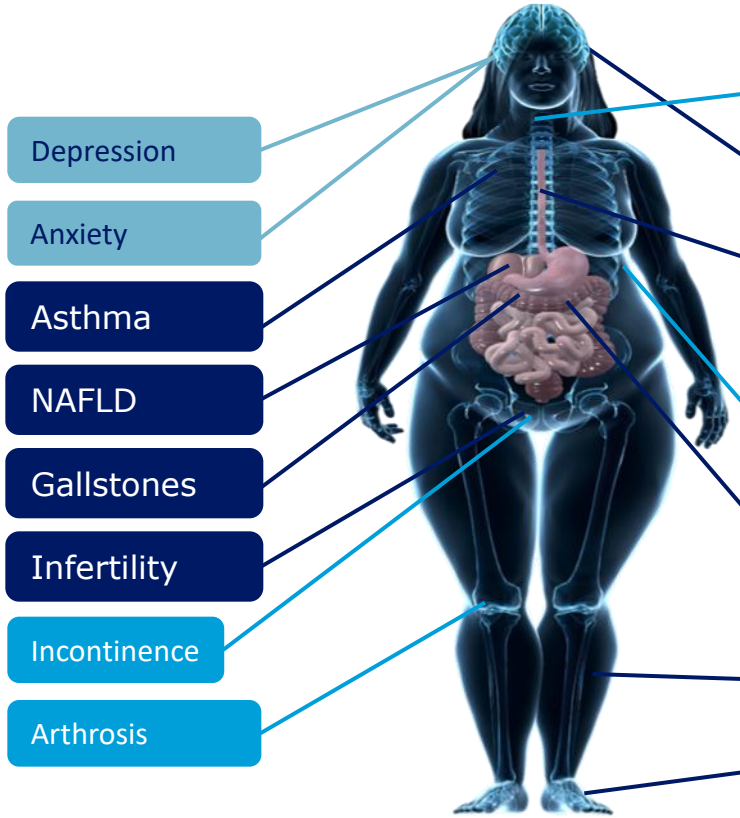


*Based on a meta-analysis of 57 international prospective studies predominantly based in Europe, the United States, Israel and Australia, including BMI
information for 894,576 adults. BMI, body mass index

Prospective Studies Collaboration. Lancet 2009;373:1083–96

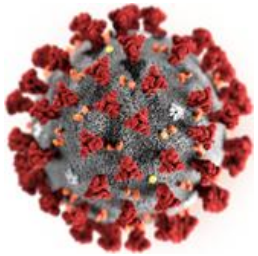
Obesity is associated with multiple comorbidities and complications

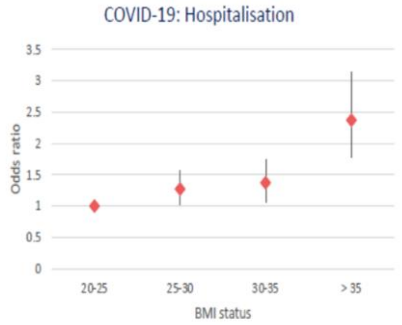
- Metabolic
- Mechanical
- Mental
- Cancers*
- Physical functioning



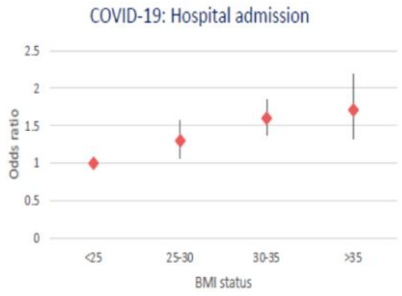
- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Infertility
- Incontinence
- Arthrosis

- Sleep apnoea
- CVD and risk factors
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - Congestive heart failure
  - Pulmonary embolism
- Chronic back pain
- Type 2 diabetes
  Prediabetes
- Thrombosis
- Gout





Source: Hamer, Gale et al, 2020 (UK) (n=334,329)

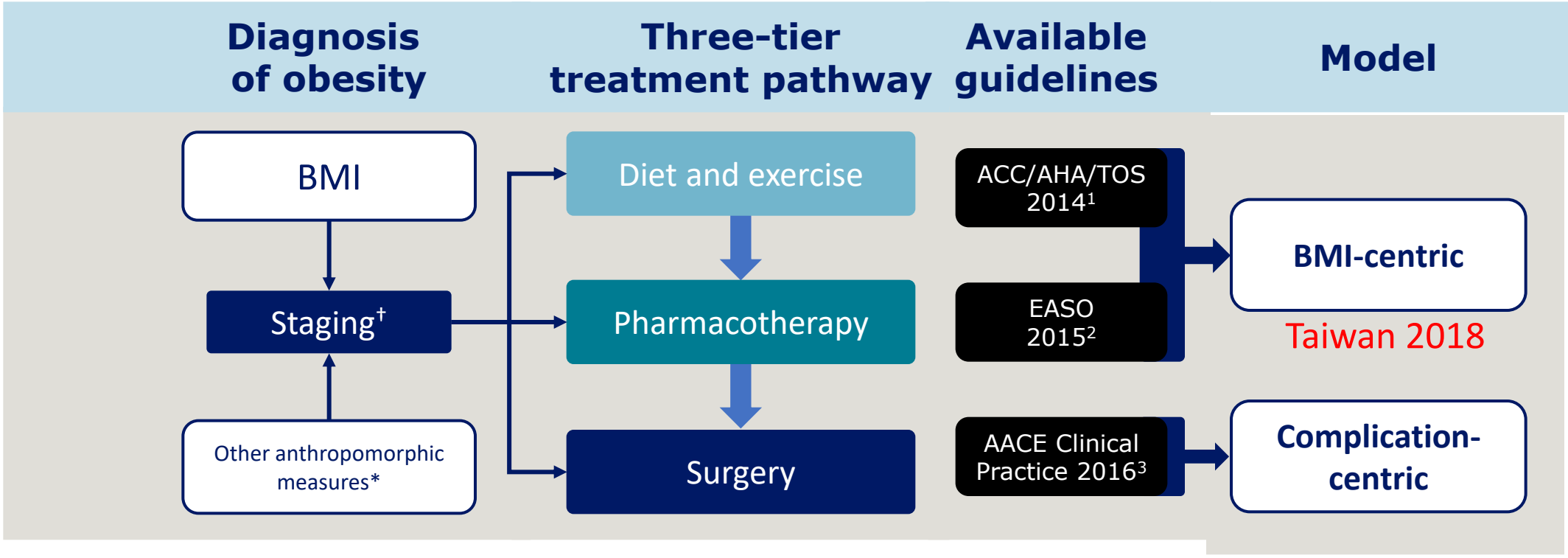


Source: Petrilli et al, 2020 (New York)(n=5279)

CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease
*Including breast, colorectal, endometrial, esophageal, kidney, ovarian, pancreatic and prostate

Adapted from Sharma AM. *Obes Rev*. 2010;11:808-9; Guh *et al*; Luppino *et al. Arch Gen Psychiatry* 2010;67:220–9; Simon *et al. Arch Gen Psychiatry* 2006;63:824–30; Church *et al. Gastroenterology* 20. *BMC Public Health* 2009;9:8806;130:2023–30; Li *et al. Prev Med* 2010;51:18–23; Hosler. *Prev Chronic Dis* 2009;6:A48

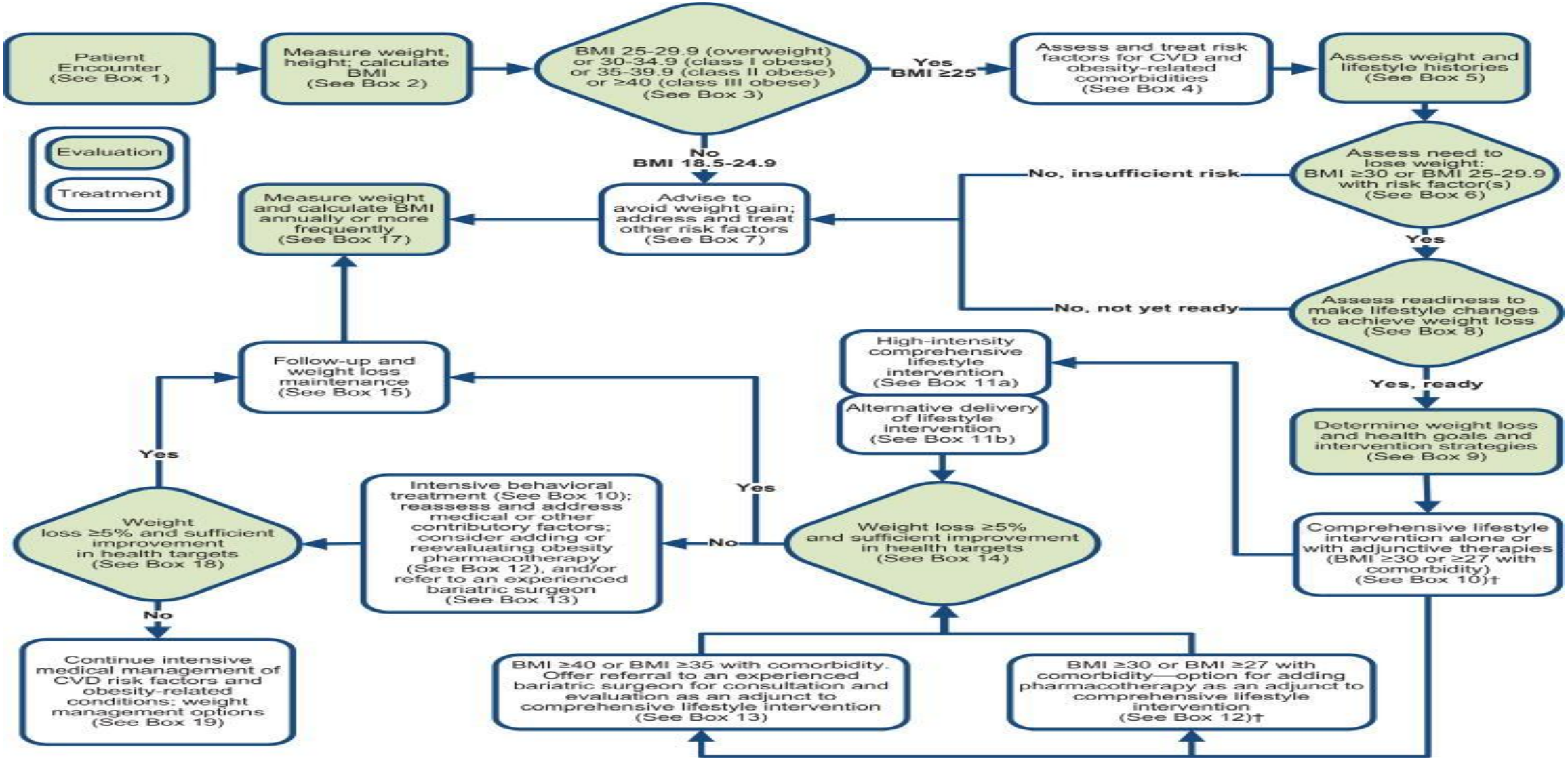
Guidelines describe obesity treatment pathway



*Other measures include waist circumference and body composition assessments. †Optional step

1. Jensen *et al*. *Circulation* 2014;129(25 Suppl 2):S102–38; 2. Yumuk *et al. Obes Facts* 2015;8:402–424; 3. Garvey *et al*. *Endocr Pract* 2016;22(Suppl 3):1–203

AHA/ACC/TOS guideline for the management of overweight and obesity in adults



Obesity treatment guidelines

> One size does not fit all

Patients with obesity are diverse

- Age, sex, race/ethnicity, genetics, complications, concomitant medications, weight, body fat distribution, socioeconomic status, culture, personal preferences, etc.

Heterogeneity of treatment effects

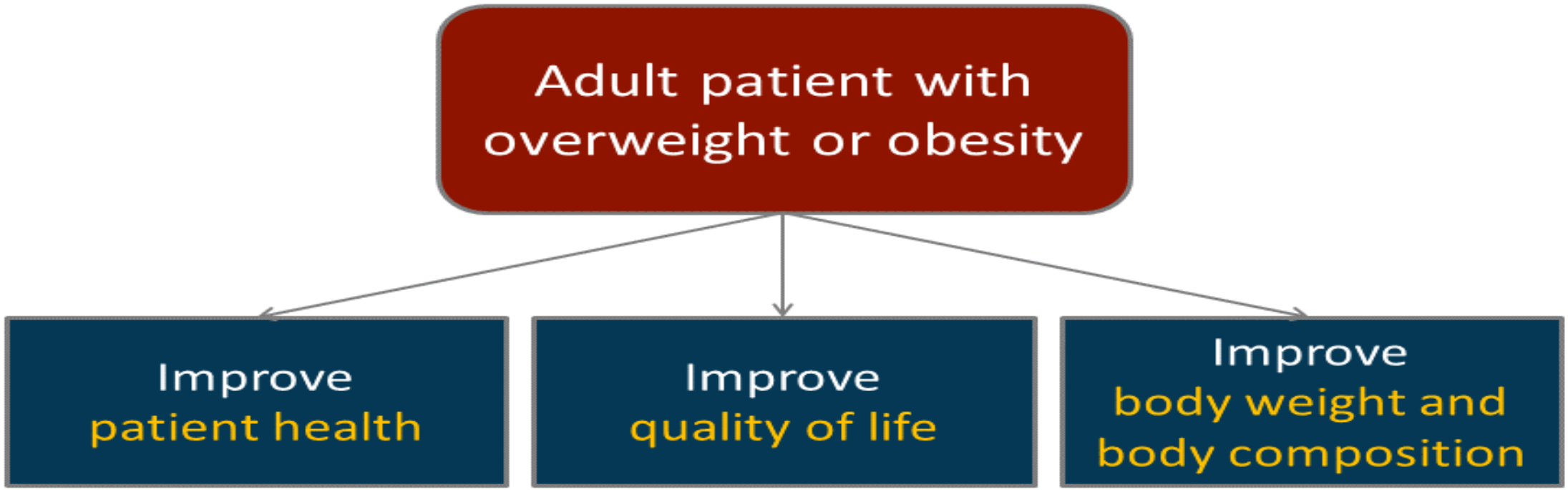
- Great variation in weight loss efficacy response – true for all weight loss treatments (lifestyle, surgery, pharmacotherapy)
- Some patients may be susceptible to adverse effects of a treatment, thus achieving fewer health benefits
- Some treatments may have weight-loss-independent health benefits, thus some patients may achieve additional health benefits

Treatment approaches must be individualised

IDF, International Diabetes Federation; T2D, type 2 diabetes; WL, weight loss

IDF. Clinical practice recommendations for managing T2D in primary care. Available here

Overall Obesity Management Goals: Set Realistic Expectations With Your Patients



Seger JC, et al. www.obesityalgorithm.org. Accessed April 22, 2015.

ASSESS

Assess for Obesity Drivers, Complications, and Barriers

- Use the 4Ms framework to assess Mental, Mechanical, Metabolic, and Monetary drivers, complications, and barriers to weight management.

The 4Ms of Obesity

Mental

Cognition
Depression
Attention Deficit
Addiction
Psychosis
Eating Disorder
Trauma
Insomnia

Mechanical

Sleep Apnea
Osteoarthritis
Chronic Pain
Reflux Disease
Incontinence
Thrombosis
Intertrigo
Plantar Fasciitis

Metabolic

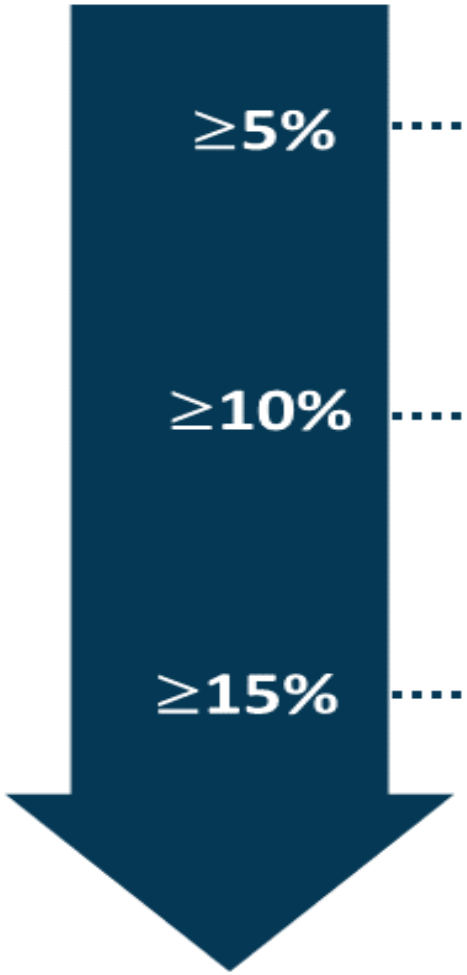
Type 2 Diabetes
Dyslipidemia
Hypertension
Gout
Fatty Liver
Gallstones
PCOS
Cancer

Monetary

Education
Employment
Income
Disability
Insurance
Benefits
Bariatric Supplies
Weight-Loss Programs

5As of Obesity Management © 2012 Canadian Obesity Network

How Much Weight Provides Benefits?



≥5% — T2DM prevention; with T2DM – better glycemic control/ medication reduction; improvement in urinary stress incontinence, mobility, joint pain, weight-related quality of life; improvements in CVD risk factors (HDL-C, triglycerides, BP)

≥10% — Previous improvements; improvements in sleep apnea; ? T2DM remission

≥15% — Previous improvements; reductions in CVD events; reductions in all-cause mortality and reduction in cancer risk (with surgical weight loss)

Weight loss–associated morbidity: Cardiac arrhythmias, electrolyte derangements (hypokalemia, etc.), hyperuricemia, psychological sequelae (depression, eating disorders, etc.), cholelithiasis

Blackburn G. *Obes Res*. 1995;3(suppl 2):211s-216s; Foster GD, et al. *Arch Intern Med*. 2009;169:1619-1626
Greg EW, et al. *JAMA*. 2012;308:2489-2496; Sjostrom L, et al. *J Intern Med*. 2013;273:219-234
Christou NV, et al. *Surg Obes Relat Dis*. 2008;4:691-695; Wing RR, et al. *J Urol*. 2010;184:1005-1010.

Obesity care is about health, not weight. Weight loss is just one outcome of obesity care

International Obesity Collaborative

CONSENSUS STATEMENT

Obesity Care vs. Weight Loss

Obesity care and weight loss are not the same.

Obesity care delivered by qualified clinicians consists of evidence-based options that address comorbidities of obesity (diabetes, hypertension, hyperlipidemia, etc.) and improve well-being. Obesity care is about health, not weight. Weight loss is just one outcome of obesity care.

Obesity is a serious, relapsing chronic disease that requires long term care, just like any other chronic disease. Safe and effective evidence-based obesity treatments that improve patient health are available.

Evidence-based treatments for obesity and severe obesity may include: nutrition and behavior modification, physical activity, medications, approved devices, and metabolic/bariatric surgery. In decisions shared with patients, clinicians utilize one or more of these modalities to treat obesity.

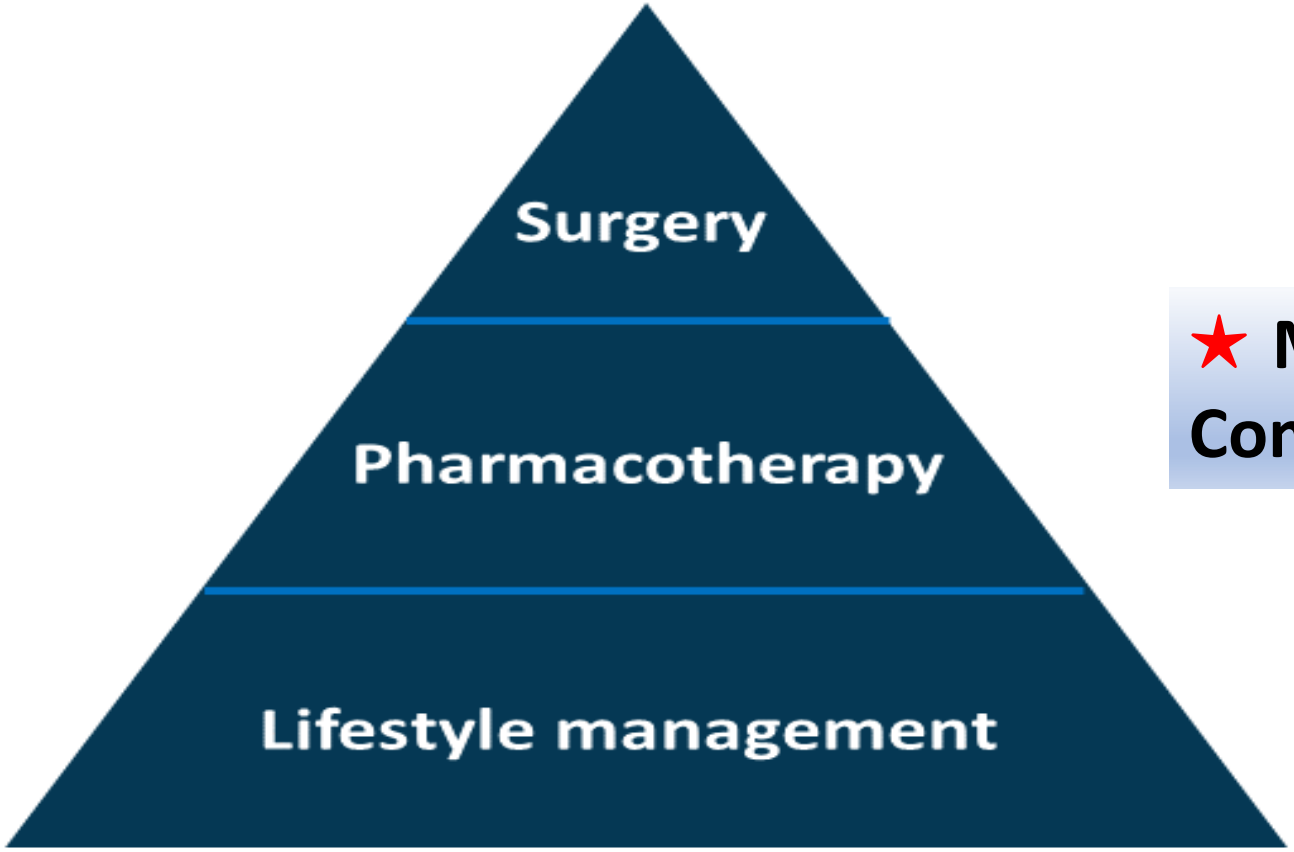
Globally, medical coverage limits access to effective obesity care, to the detriment of patient health. National statutes and medical insurance coverage have not kept pace with evidence and advances in clinical science. Like other serious chronic diseases, support for obesity care must be incorporated into national public health strategies and include standard benefits and coverage for obesity across the lifespan.

People with obesity deserve care, free from stigma and shame.

International Obesity Collaborative Members

OAC · ASMBS · EASO · eat right. · GOPA · obesity canada · obésité canada · Obesity Medicine Association · SOPHIA · STOP OBESITY · THE OBESITY SOCIETY · ECPO · KSO

Treatment Options for Overweight and Obesity



★ **Management of Comorbidities**

Seger JC, et al. www.obesityalgorithm.org. Accessed April 22, 2015.
Jensen MD, et al. *Circulation*. 2014;129(25 suppl 2):S102-S138
Apovian CM, et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

Adapted from Medscape

Lifestyle Management of Obesity

- Self-monitoring of caloric intake (balanced low-calorie diets and diets with different macronutrient compositions) and physical activity(30-60 minutes of continuous aerobic exercise 5-7 times per week)
- Goal setting
- Stimulus control
- Nonfood rewards
- Relapse prevention

Obesity Treatment & Management. Medscape Oct 4, 2024

Anti-obesity medications (AOMs)

1 Centrally Acting Medications

Phentermine

Primarily increases norepinephrine

- Reduces appetite
- Adverse effects may include xerostomia, insomnia, headache, and constipation

Phentermine-topiramate

Increases norepinephrine, augments GABA, and inhibits AMPA/kainite excitatory glutamate receptors

- Reduces appetite
- Adverse effects may include paresthesia, xerostomia, constipation, and dysgeusia

Naltrexone-bupropion

Stimulates proopiomelanocortin neurons

- Reduces appetite
- Adverse effects may include nausea, constipation, headache, vomiting, dizziness, insomnia, and xerostomia

2 Nutrient-Stimulated Hormone (Incretin)-Based Medications

Liraglutide, semaglutide (GLP-1 receptor agonists)

Tirzepatide (GIP/GLP-1 receptor agonist)

Simulate metabolic effects of enteropancreatic hormones via the gut-brain axis

- Reduces appetite
- Adverse effects may include nausea, diarrhea, vomiting, constipation, and abdominal pain

3 Intragastrointestinal Medications

Orlistat

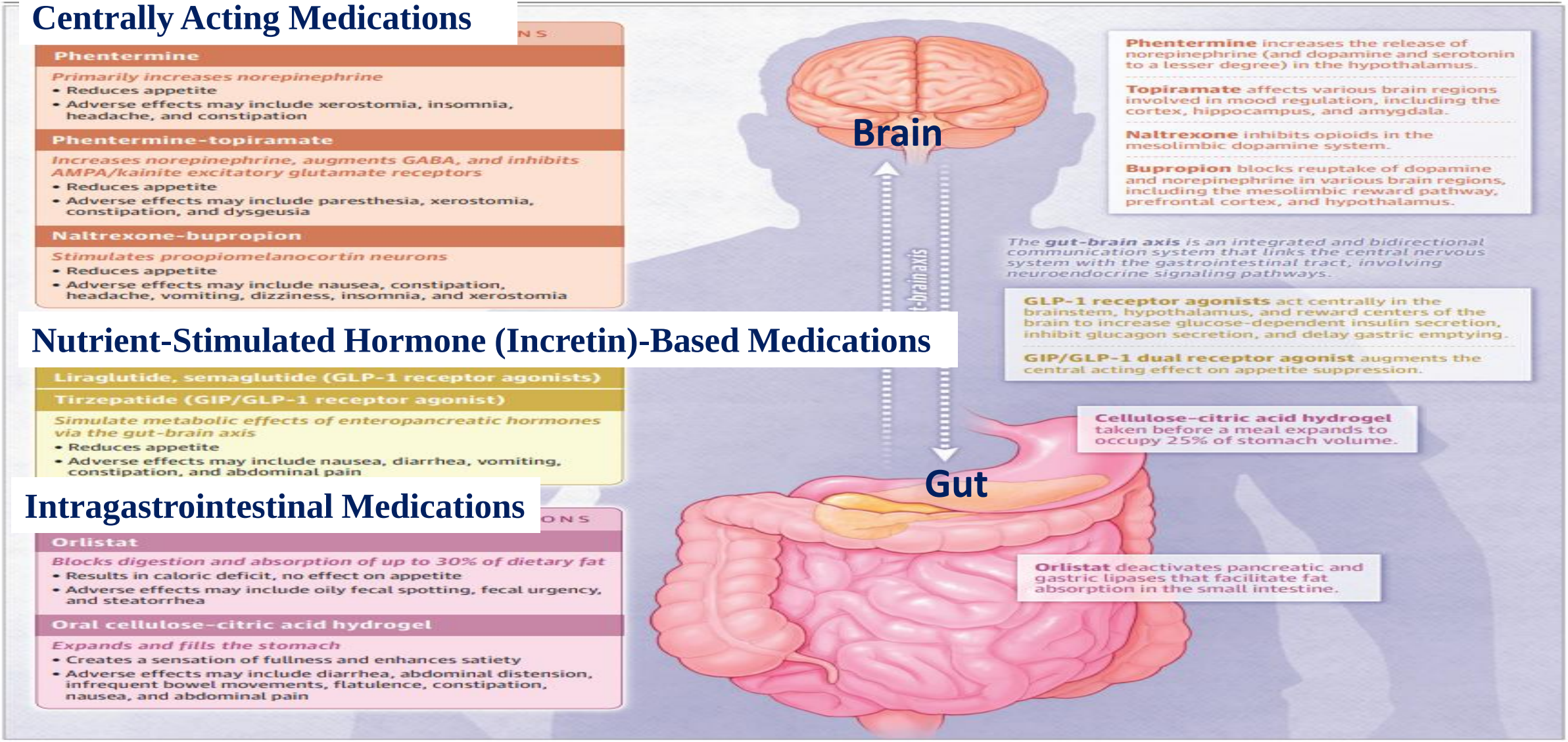
Blocks digestion and absorption of up to 30% of dietary fat

- Results in caloric deficit, no effect on appetite
- Adverse effects may include oily fecal spotting, fecal urgency, and steatorrhea

Oral cellulose-citric acid hydrogel

Expands and fills the stomach

- Creates a sensation of fullness and enhances satiety
- Adverse effects may include diarrhea, abdominal distension, infrequent bowel movements, flatulence, constipation, nausea, and abdominal pain



AMPA indicates α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GABA, γ-aminobutyric acid; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide 1.

JAMA. 2024;332(7):571-584.

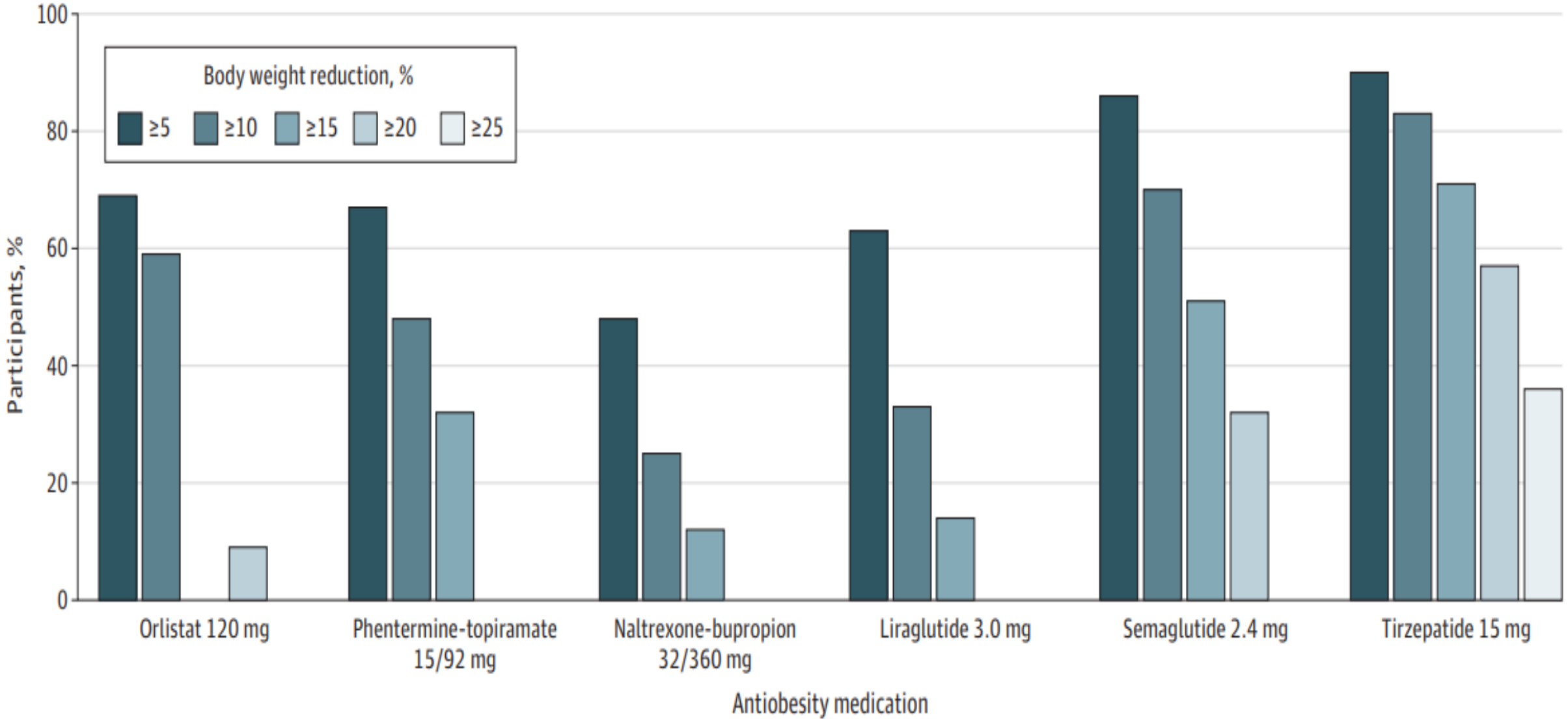
Anti-Obesity Medications

FDA-approved for obesity treatment
Orlistat
Phentermine
Phentermine / Topiramate
Bupropion / Naltrexone
Liraglutide 3mg
Semaglutide 2.4mg ***Tirzepatide***
Setmelanotide *monogenic obesity**

Additional medications used	
Metformin	
Topiramate	
Zonisamide	
Bupropion	
Naltrexone	
GLP-1a	**Dulaglutide** **Liraglutide** **Exenatide** **Semaglutide** **Lixisenatide**
Pramlintide	
SGLT2i	**Canagliflozin** **Dapagliflozin** **Empagliflozin**

* POMC, PCSK1, LEPR deficiency

Figure 2. Percentage of Adults With Obesity Without Diabetes Achieving Specific Weight-Loss Targets by Antiobesity Medication



JAMA. 2024;332(7):571-584.

Table 1. Weight and Cardiovascular Risk Factor Outcomes[a] of Antiobesity Medications in Adults With Obesity and Without Diabetes by Mechanism of Action

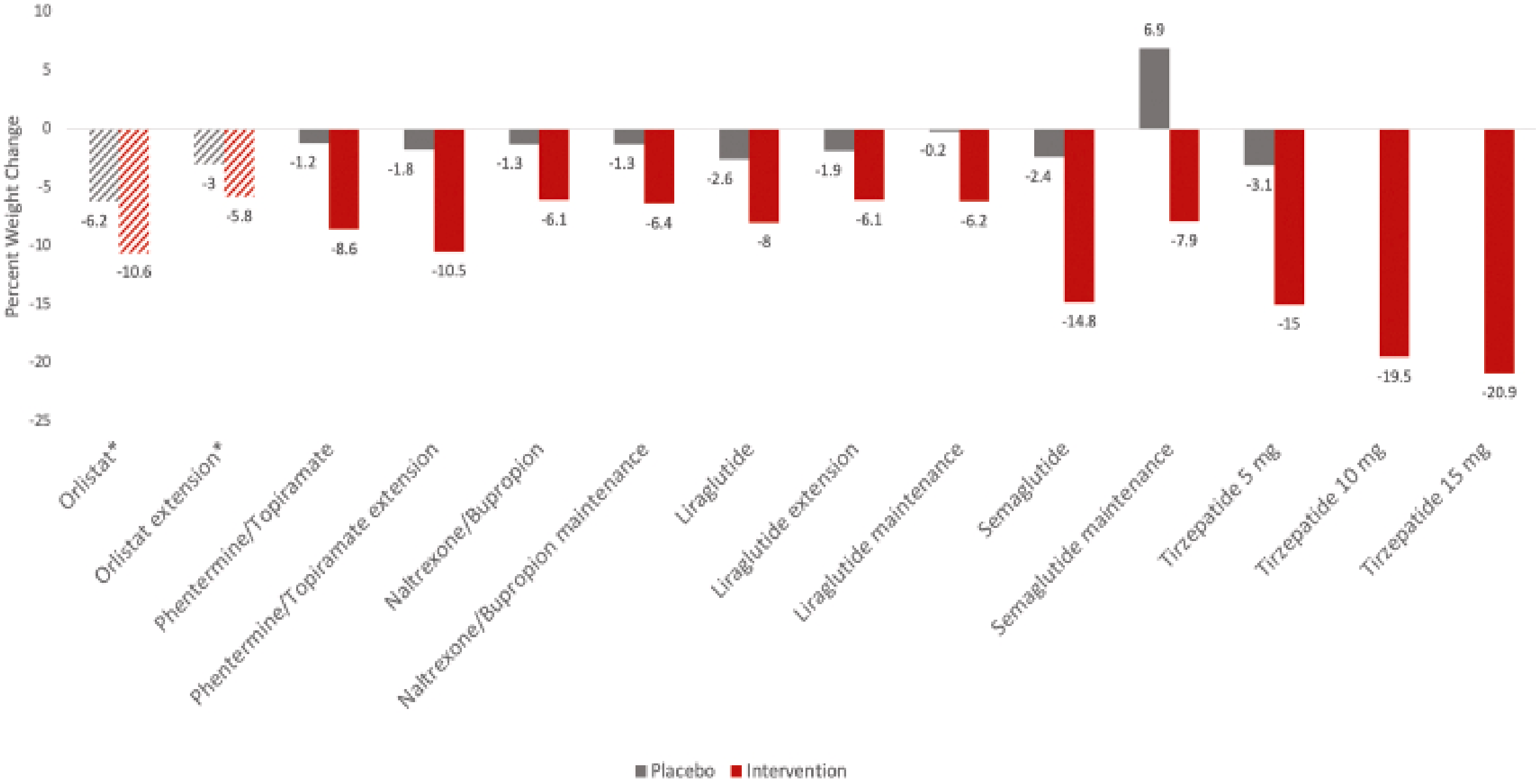
Intragastrointestinal Medications

Centrally Acting Medications

Nutrient-Stimulated Hormone (Incretin)-Based Medications

Mechanism of action group	Antiobesity medication	Time point, mo	Mean weight change, %	Mean systolic blood pressure change, mm Hg	Mean LDL-C change, %	Mean waist circumference change, cm	Common adverse effects	Mechanism of action
Intragastrointestinal medications	Orlistat[12,16,23]	12	−10.2	−6	−9.4	−9.6	Oily fecal spotting (27%), flatus with discharge (24%), fecal urgency (22%), steatorrhea (20%), oily discharge (12%), increased defecation (11%)	Intestinal lipase inhibitor
Centrally acting medications	Phentermine[24]	6	−6.1[b]	−6.4[b]	Not reported	−6.6[b]	Xerostomia (12%), insomnia (11%), headache (10%)	Sympathomimetic amine
	Phentermine-topiramate[17,25]	12	−10.9	−2.9	−8.4	−10.9	Paresthesia (20%), xerostomia (19%), constipation (16%), headache (11%)	Sympathomimetic amine combined with GABA augmentation
	Naltrexone-bupropion[18,26]	12	−6.1	−0.1[c]	−2.0[d]	−6.2	Nausea (33%), constipation (19%), headache (18%), vomiting (11%), dizziness (10%)	POMC neuron stimulation
Nutrient-stimulated hormone-based medications	Liraglutide[19,27]	12	−8.0	−4.2	−3.0	−8.2	Nausea (39%), diarrhea (21%), constipation (19%), vomiting (16%), injection site reaction (14%), headache (14%), dyspepsia (10%)	GLP-1 receptor agonist
	Semaglutide[20,28]	16	−14.9	−6.2	Not reported[e]	−13.5	Nausea (44%), diarrhea (30%), vomiting (24%), constipation (24%), abdominal pain (20%), headache (14%), fatigue (10%)	GLP-1 receptor agonist
	Tirzepatide[21,29]	17	−20.9	−7.6	−8.6	−18.5	Nausea (28%), diarrhea (23%), vomiting (13%), constipation (11%), abdominal pain (10%), dyspepsia (10%)	GIP/GLP-1 receptor agonist

JAMA. 2024;332(7):571-584.

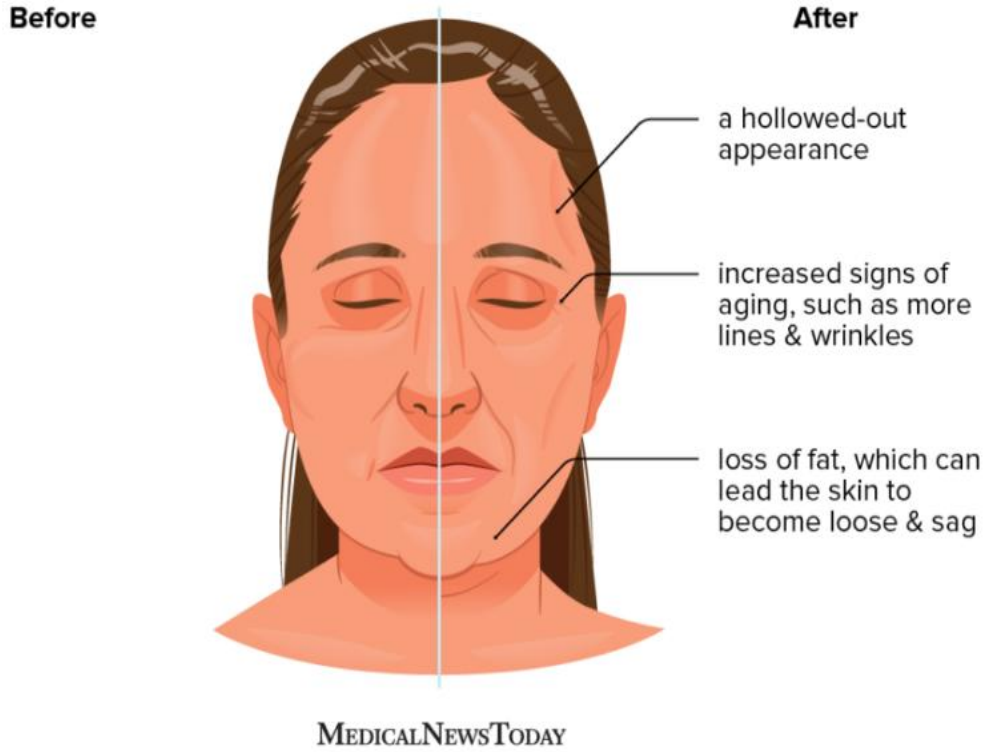


eClinicalMedicine. 2023 Apr; 58: 101882.

Table 2. Individualizing Selection of Antiobesity Medications Among Specific Populations With Obesity Common in Primary Care Settings[a]

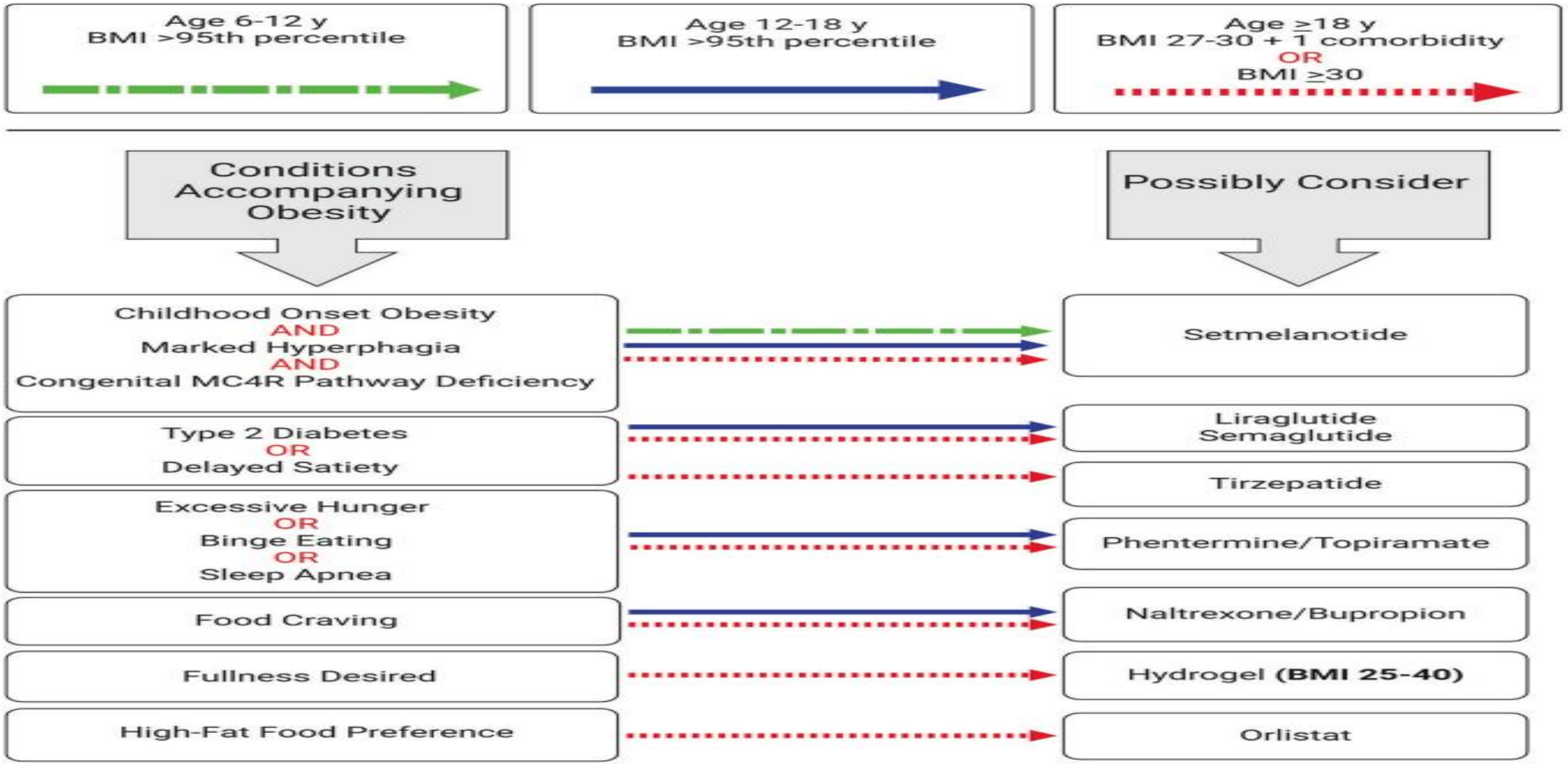
Medication	Depression/anxiety	CAD	HTN	Type 2 diabetes	Moderate kidney impairment[b]	Mild-moderate hepatic impairment[c]	Older adults (>65 y)[d]
Orlistat[12]	Use	Use	Use (lower BP)[30]	Use (lower A_{1c})[31]	Use	Use with caution; monitor cholelithiasis	Limited data
Phentermine[32,33]	Use with caution; limited data	No	Use with caution; baseline BP controlled; limited data	Unknown	Unknown	Unknown	Unknown
Phentermine-topiramate[25]	Use with caution; avoid maximum dose (15/92 mg) to decrease risk of adverse mood effects	Use with caution; monitor HR	Use (lower BP)[30]	Use (lower A_{1c})[34]	Limit dose to 7.5/46 mg daily	Limit dose to 7.5/46 mg daily	Limited data
Naltrexone-bupropion[26]	Unknown; avoid in young adults	Use with caution; monitor BP/HR	Use with caution; baseline BP controlled; monitor BP/HR	Use (lower A_{1c})[35]	Limit dose to 8/90 mg daily	Limit dose to 8/90 mg daily	Limited data
Liraglutide[27]	Use; monitor mood	Use; monitor HR	Use (lower BP)[19]	Use (lower A_{1c})[36]	Use	Use with caution; limited data	Limited data
Semaglutide[28]	Use; monitor mood	Use; monitor HR	Use (lower BP)[20]	Use (lower A_{1c})[37]	Use	Use; monitor cholelithiasis	Limited data
Tirzepatide[29]	Use; monitor mood	Unknown	Use (lower BP)[21]	Use (lower A_{1c})[38]	Use	Use; monitor cholelithiasis	Limited data

JAMA. 2024;332(7):571-584.



"***Ozempic face***" is a term for common side effects of the medication "semaglutide (Ozempic)". It can cause sagging and aging of facial skin. You may recommend lifestyle modifications or facial fillers to treat skin and facial side effects.

An algorithm for the use of anti-obesity medications

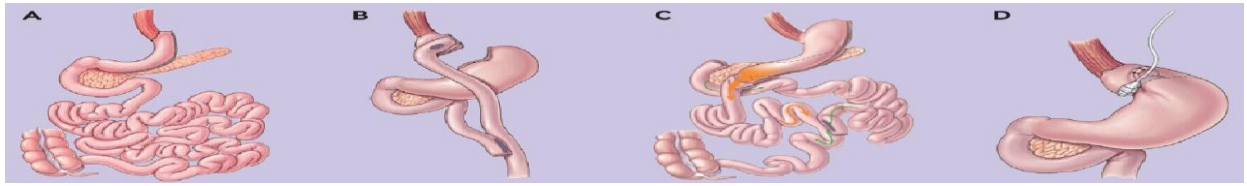


Nutrition and Diabetes (2024) 14:20

Bariatric (Metabolic) Surgery

- Previously, BMI ≥40, or BMIs of 35-40 with at least 1 major comorbidity were indicated for bariatric surgery
- Now, BMI ≥35 kg/m2 regardless of co-morbidities and 30-34.9 kg/m2 with obesity-related comorbidities are for bariatric surgery
- Lower weight thresholds should be applied to Asian populations
- **Bariatric (Metabolic) surgery results in durable and significant weight loss and improvements in comorbid conditions**
- In the PCORNet Cohort Study (n = 65,093), weight losses at 1 year with RYGB and sleeve gastrectomy were 31.2% and 25.2%, respectively. Weight losses after 5 years were 25.5% and 18.8%, respectively

Ann Intern Med. 2018;169:741-750; BMJ. 2023 Dec 18:383:e071027



American Society for Metabolic and Bariatric Surgery (ASMBS)2022 and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO)

Recommended postoperative screening and follow-up

- **Monitor progress with weight loss and weight regain; consider evaluation by bariatric medicine provider, nutrition/medications if regain occurs**
- **Avoid non-steroidal anti-inflammatory drugs (NSAIDs)**
- **Consider gout and gallstone prophylaxis**
- **Screen annually for depression and alcohol and substance use disorders; refer for treatment as needed**
- **Encourage long term daily bariatric formulation vitamin supplementation to reduce risk of nutritional deficiencies**
- **Annual nutritional monitoring, including 24 hour urine calcium excretion (for biliopancreatic diversion), vitamin B12, folic acid, iron studies, 25-hydroxy vitamin D, intact parathyroid hormone**
- **Bone density screening (dual x ray absorptiometry) every two years**

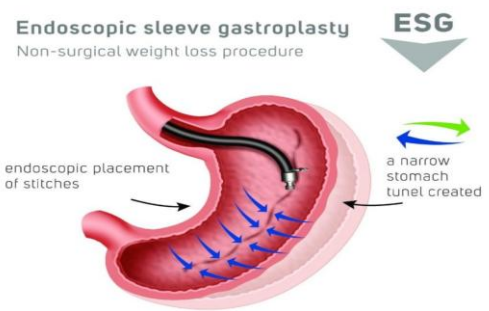
BMJ 2023;383:e071027

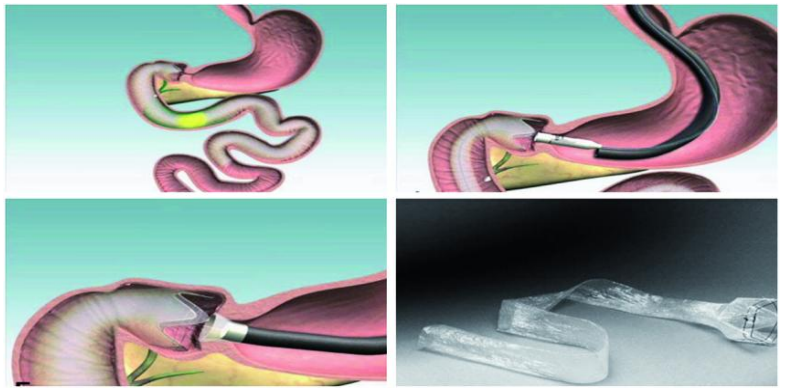
Endoscopic Bariatric Therapies

Types of EBT		
Space-Occupying Devices	Procedures	
	Stomach	Small Bowel
Intra-gastric balloons*	Primary Obesity Surgery Endoluminal (POSE)*	Duodenal Jejunal Bypass Sleeve (Endobarrier)*
Transpyloric Shuttle	Endoscopic Sleeve Gastroplasty (ESG)*	Gastroduodenal-Jejunal Bypass (Endobypass system)*
The Full Sense	Transoral Outlet Reduction	Duodenal Mucosal Resurfacing (DMR)
Hydrogels		Incisionless Magnetic Anastomosis System (IAS)*
Aspiration Therapy (Aspire Assist)*		
Botulinum Toxin Injection		

15% at 6 months, 16% at 12 months, and 17% at 24 months

10-15% upon removal of the balloon (6 months) and 6-8% at 12 months





JSLS. 2022 Jan-Mar;26(1):e2021.00066.

Approach	Eligible patients[b]	Description or examples	Mean weight loss at 12-24 mo[c]	Other considerations
Multicomponent intensive behavioral lifestyle interventions[13]	• BMI ≥30 • BMI ≥25 with obesity-associated comorbidity[d]	• Evidence-based approaches include goal setting, self-monitoring (eg, food intake, physical activity, daily body weight), dietary change, stimulus control, stress management, cognitive therapy[13,14] • Multicomponent interventions combine these approaches and are delivered by trained facilitators, often referred from a primary care setting[13] • Intensive programs are administered over 1-2 y with ≥12-14 sessions in 6 mo[5] (see Table 3 for examples of programs)	1%-9%[4,5,13]	Higher intensity of weight loss instruction is associated with greater weight loss vs low- and moderate-intensity interventions[4]
Nutritional intervention	• BMI ≥30 • BMI ≥25 with obesity-associated comorbidity[d]	• Restricting/eliminating certain types of foods to create calorie deficit[5] • Generally 1200-1500 kcal/d for women and 1500-1800 kcal/d for men[5]; very low-calorie diets (<800 kcal/d) require specialized medical supervision[5] • Clinicians can provide counseling or refer to dietician • See more details on 3 evidence-based diet patterns in Table 3	3%-8%; 10% with very low-calorie diets[47]	Specific dietary recommendations need to account for patient preference and potential for long-term adherence
Physical activity	All adults regardless of BMI[40]	• ≥150 min/wk moderate-intensity physical activity (30 min 5 times per wk), or 75-150 min/wk vigorous-intensity physical activity[40] • Resistance exercise 2-3 times per wk[4] • >200 min/wk is associated with better maintenance of weight loss[5]	1%-3%[4]	Exercise should be individualized to patients' health and physical limitations and increased as patient is able to tolerate intensity to reach goals[4]
Pharmacotherapy[e]	• BMI ≥30 • BMI ≥27 with obesity-associated comorbidity[5] • Consider with inadequate response to lifestyle therapy and/or presence of mild to moderate obesity complications[4]	Medications vary in terms of administration and dosage (minimum-maximum dose): • FDA approved for long-term use • Semaglutide (0.25-2.4 mg/wk subcutaneously) • Phentermine-topiramate ER (3.75/23 mg/d to 15/92 mg/d orally) • Liraglutide (0.6-3 mg/d subcutaneously) • Naltrexone-bupropion ER (8 mg/90 mg daily to 16 mg/180 mg twice daily orally) • Orlistat (60-120 mg 3 times daily orally) • FDA approved for short-term use • Diethylpropion (IR: 25 mg 3 times daily; ER: 75 mg/d orally) • Phentermine (8 mg/d to 8 mg 3 times daily or 15-37.5 mg/d orally) • Commonly used off label • Tirzepatide (2.5-15 mg/wk subcutaneously) • Semaglutide (3-50 mg/d orally) (50-mg/d oral dose not yet available) • Topiramate (12.5-200 mg/d in 1 to 2 divided doses) • Semaglutide (0.25-2.0 mg/wk subcutaneously) • Liraglutide (0.6-1.8 mg/d subcutaneously) • Bupropion (SR: 100-200 mg twice daily orally; ER: 150-450 mg/d orally) • Metformin (500-2500 mg/d orally)	5% (naltrexone-bupropion, 32 mg/360 mg daily)[41] to 21% (tirzepatide, 15 mg once weekly)42[f]	• See Table 4; adverse effects can often be avoided with slow dose titration or reducing dose to last tolerated dose • Administer concurrent with lifestyle interventions
Metabolic and bariatric surgery	• BMI ≥35 • BMI ≥30 with obesity-associated comorbidity[9] • Consider with inadequate response to lifestyle therapy	• Laparoscopic sleeve gastrectomy: approximately 85% of stomach removed by separation along greater curvature[43] • Roux-en-Y gastric bypass: small gastric pouch connected directly to jejunum[43]	25%-35%[5,44]	• Major complications <5%[44,45] • Long-term monitoring necessary for risks related to nutritional deficiency and bone health[45] • Administer concurrent with lifestyle interventions

1-10%

5-21%

25-35%

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Summary

Percent total body weight loss (TBWL)

5%
10%
15%
20%
25%
30%
35%

Intensive lifestyle therapy

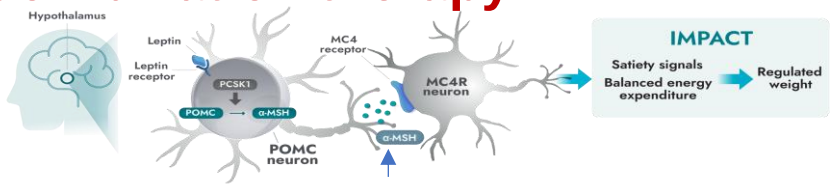
Current Pharmacotherapy

naltrexone/bupropion, phentermine, liraglutide 3mg, phentermine/topiramate

Treatment Gap

Bariatric surgery, EBT

Combination therapy



Setmelanotide(IMCIVREE)

New Pharmacotherapy

semaglutide 2.4mg (FDA-approved June 2021)

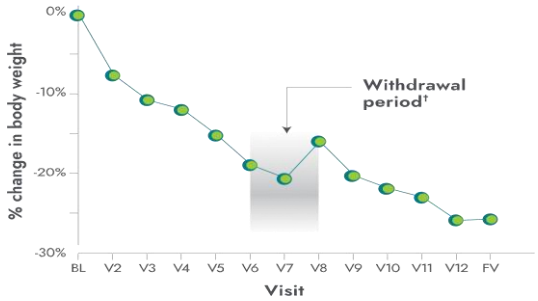
tirzepatide (GIP/GLP-1a – FDA-approved Nov 2023)

cagrilintide-sema (amylin-GLP1a – Phase 3)

danuglipron (GLP-1a small molecule – Phase 2b)

AMG133 (maridebart cafraglutide-MariTide)

setmelanotide (FDA-approved – *monogenic obesity*)



Slide: Ania Jastreboff, MD, PhD

TBWL = total body weight loss

* POMC, PCSK1, LEPR deficiency


thank you