Oral anti-obesity medications (AOMs)

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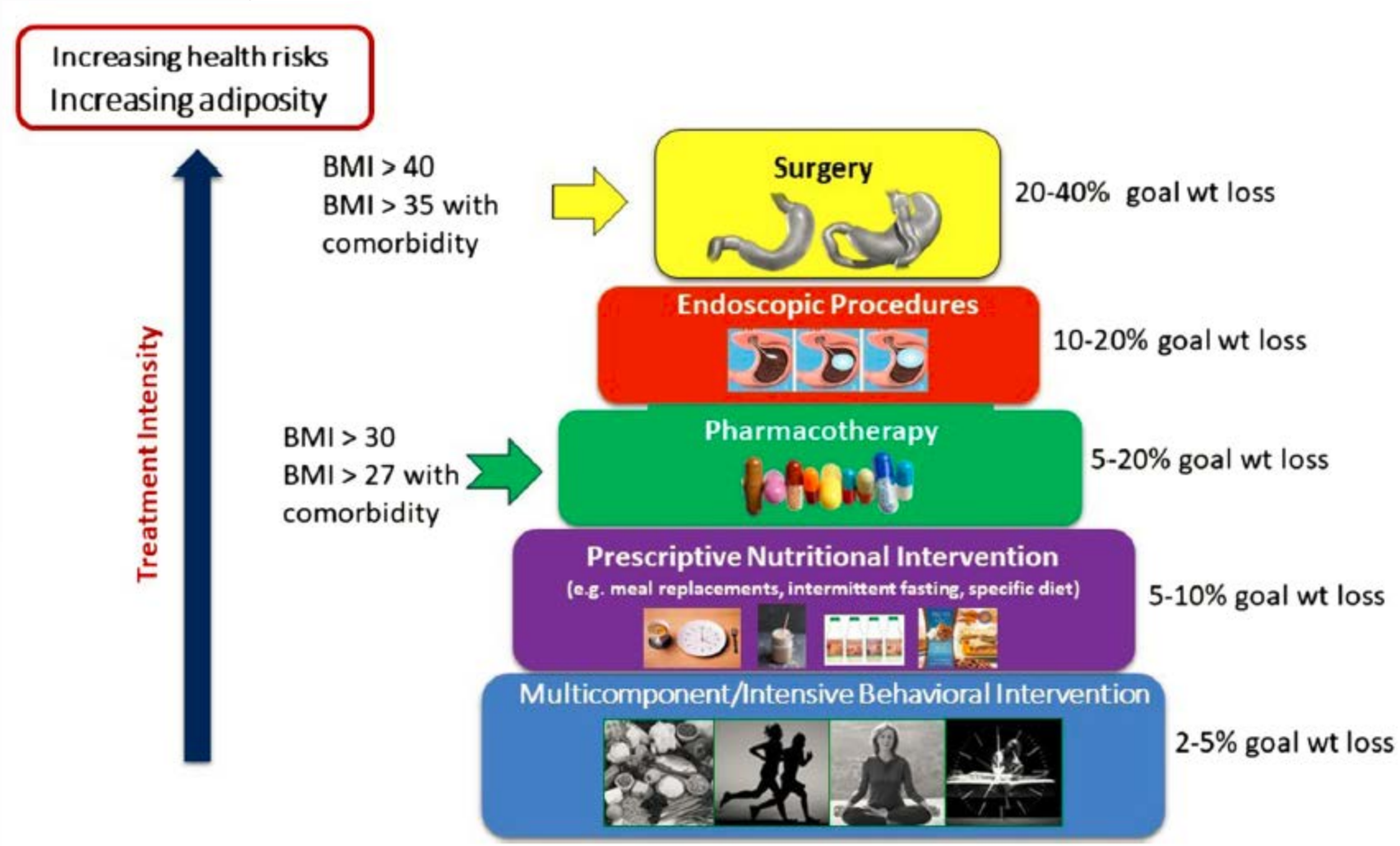
Agenda

- Obesity treatment pyramid
- Timeline of AOM
- AACE/ACE & ADA guideline
- Medication for adult
- Target of anti-obesity drugs
- Medication for adolescent
- Key massage

Obesity Treatment Pyramid



Currents obesity reports, 2021

Overweight and Obesity Classification by BMI from CDC

Metric:

BMI = kilograms / meters^2

US customary and imperial:

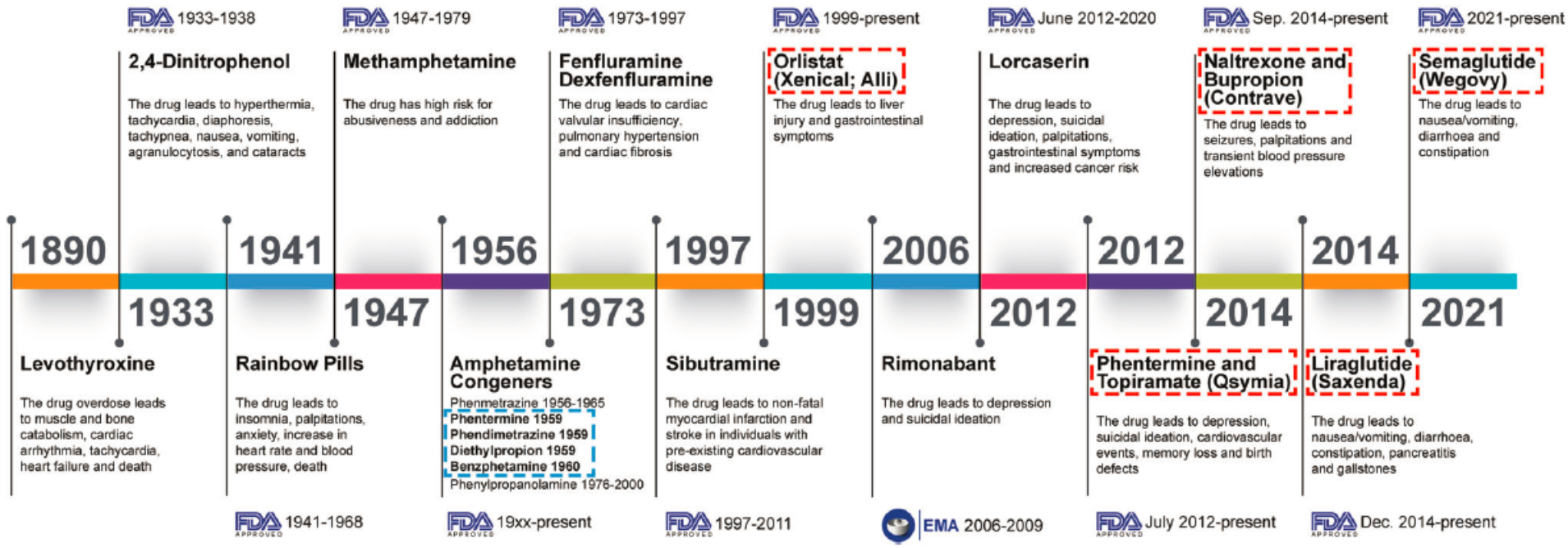
BMI = lb * 703 / *in*^{2}

BMI range	Weight class
< 18.5 kg/m^2	Underweight
18.5 to < 25 kg/m^2	Normal weight
25.0 to < 30 kg/m^2	Overweight
30 to < 35 kg/m^2	Class 1 obesity
35 to < 40 kg/m^2	Class 2 obesity
≥ 40 kg/m^2	Class 3 obesity

BMI, body mass index. a BMI is screening tool, but it does not diagnose excess adiposity or provide a health assessment. Repurposed from the Centers for Disease Control and Prevention (CDC). Use of this figure does not imply the CDC's endorsement of the material contained in this publication. This figure and related material are available, free of charge, at http://www.cdc.gov.

Defining adult overweight & obesity. Centers for Disease Control and Prevention. Reviewed June 3, 2022. Accessed October 7, 2022. https://www.cdc.gov/obesity/adult/defining.html

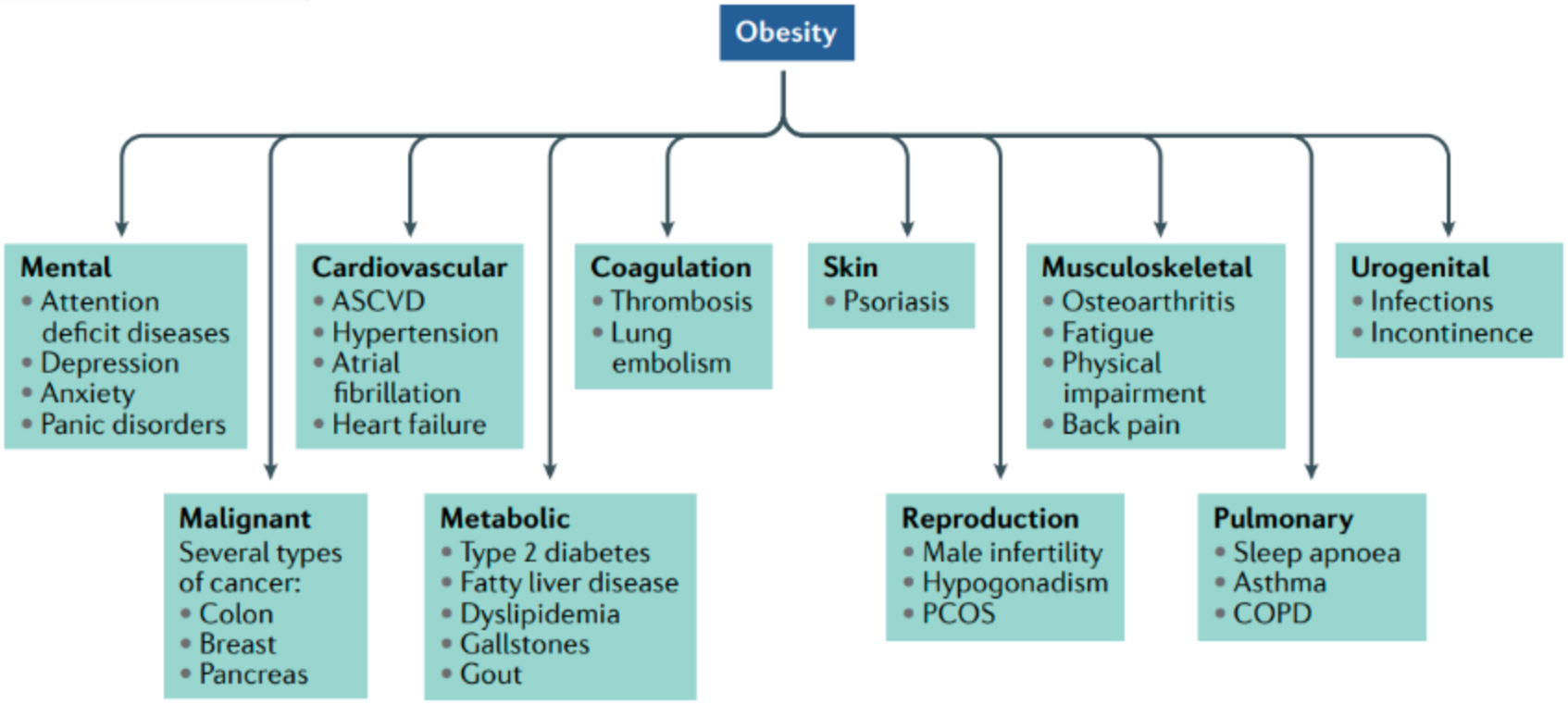
Timeline of anti-obesity medications approved by the FDA or EMA from the late nineteenth century until today



(The red dashed line indicates long-term use while the blue dashed line indicates short-term use)

Signal Transduction and Targeted Therapy (2022) 7:298

Obesity-associated metabolic disturbances



Most prominent metabolic and psychological comorbidities associated with morbid obesity. ASVCD, atherosclerotic cardiovascular disease; COPD, chronic obstructive pulmonary disease; PCOS, polycystic ovary syndrome.

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Review Article

Prevalence of Obesity and Overweight among Adults in the Middle East Countries from 2000 to 2020: A Systematic Review and Meta-Analysis

Hassan Okati-Aliabad,[1] Alireza Ansari-Moghaddam,[1] Shiva Kargar,[2] and Neda Jabbari[3]

Objective: This systematic review aimed to identify the prevalence of obesity and overweight in the Middle East region and different countries in this region.

Materials and Methods: PubMed, Google Scholar, and MEDLINE databases were searched from 2000–2020 to identify relevant studies in the Middle East area.

Trends in the Prevalence of Obesity and Overweight in Middle East countries

Country	Pooled estimate (95% CI) 2000–2006		2007–2013		2014–2020	
	Obesity Prevalence (95% CI)	Overweight Prevalence (95% CI)	Obesity Prevalence (95% CI)	Overweight Prevalence (95% CI)	Obesity Prevalence (95% CI)	Overweight Prevalence (95% CI)
Kuwait	23.53 (17.04–32.48)	44.85 (38.74–51.93)	33.95 (28.02–41.14)	41.01 (24.89–67.58)	25.27 (10.03–63.66)	29.13 (18.05–47.02)
Israel	NA	NA	22.45 (21.12–23.86)	62.1 (60.3–63.9)	NA	NA
Saudi Arabia	39.6 (37.9–41.3)	36.6 (35.0–38.3)	35.65 (23.80–53.40)	37.82 (32.64–43.83)	20.98 (16.88–26.08)	28.10 (24.18–32.64)
Oman	NA	NA	13.79 (4.79–39.45)	31.73 (29.04–34.67)	67.81 (65.22–70.51)	29.2 (23.3–35.6)
Palestine	34.71 (24.89–48.40)	36.4 (32–40.8)	24.4 (22.9–25.9)	38.0 (36.3–39.6)	16.12 (4.15–62.62)	26.39 (16.67–41.78)
Yemen	NA	NA	8.8 (7.7–10)	23.5 (22–25.2)	NA	NA
United Arab Emirates	6.7 (4.4–9.7)	19.4 (15.6–23.7)	23.91 (10.98–52.07)	29.68 (25.25–34.90)	32.15 (30.55–33.84)	39.81 (33.66–47.08)
Turkey	25.68 (22.53–29.28)	36.86 (34.93–38.90)	21.21 (16.39–27.45)	29.70 (23.50–37.54)	27.12 (21.62–34.02)	34.3 (32.2–36.4)
Qatari						
Syria	38.2 (36.0–40.3)	31.8 (29.8–33.9)	NA	NA	43.4 (40.2–46.6)	31.3 (28.3–34.4)
Lebanon	NA	NA	17.77 (3.13–100.76)	37.08 (16.08–85.50)	17.72 (11.25–27.91)	32.64 (23.46–45.40)
Iraq	25.0 (19.1–31.6)	39.0 (32.2–46.1)	13.78 (4.62–41.11)	33.01 (29.02–37.55)	43.17 (27.26–68.39)	25.69 (16.92–39.01)
Cyprus	NA	NA	29.0 (26.2–31.9)	36.0 (33.0–39.1)	18.8 (17.4–20.2)	NA
Bahrain	9.0 (6.9–11.4)	18.1 (15.2–21.3)	NA	NA	38.7 (35.7–41.5)	39.7 (36.8–42.5)
Jordan	NA	NA	23.60 (10.45–53.30)	28.63 (25.02–32.78)	15.96 (11.18–22.77)	39.94 (33.98–46.95)
Egypt	28.3 (23.6–33.3)	34.0 (29.0–39.2)	37.06 (26.83–51.21)	32.54 (31.58–33.52)	12.89 (7.17–23.16)	28.21 (26.65–29.86)
Iran	22.4 (17–27.6)	43.3 (37.6–49.1)	17.74 (12.61–24.97)	27.02 (13.28–54.94)	25.98 (22.15–30.47)	38.29 (36.0–40.72)
Sex						
Female	26.62 (22.93–30.90)	32.30 (29.84–34.96)	27.20 (23.70–31.22)	33.07 (31.17–35.09)	23.68 (21.16–26.51)	28.87 (26.97–30.91)
Male	20.08 (16.24–24.82)	39.14 (36.0–42.57)	17.09 (14.0–20.87)	36.79 (34.08–39.72)	23.48 (20.26–27.20)	39.03 (37.05–41.10)
Total (Middle East)	**23.98 (21.24–27.08)**	**34.83 (32.40–37.45)**	**22.62 (20.18–25.35)**	**32.02 (28.56–35.89)**	**23.15 (20.85–25.70)**	**32.85 (31.39–34.38)**

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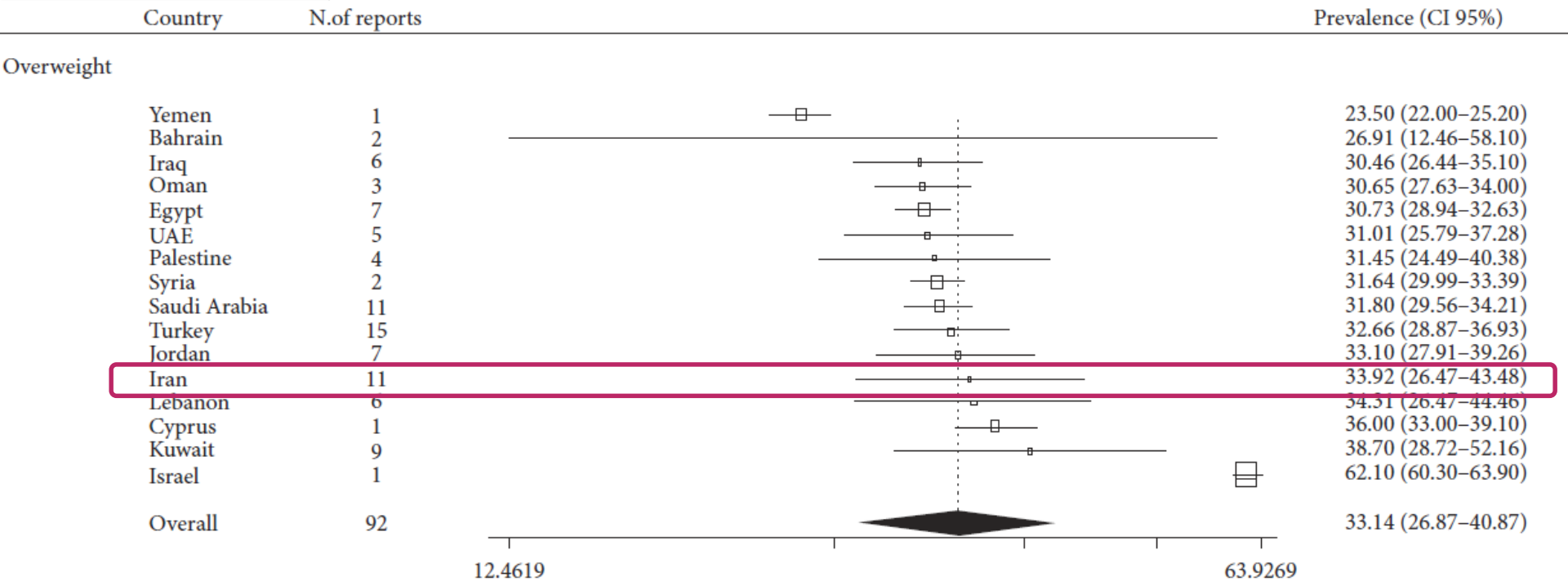
Populations Attributable Risk for Obesity by Country and Cardiovascular Diseases

Variables/PAR		Cardiovascular diseases		
		Coronary heart disease (CAD)	Heart failure (HF)	Atrial fibrillation (AF)
Countries	Kuwait	5.4 (0.4–12.5)	15.2 (7.1–25.7)	12.8 (7.1–19.2)
	Israel	4.2 (04–8.6)	6.5 (6.2–18.5)	10.0 (6.8–13.5)
	Saudi Arabia	4.5 (0.4–10.6)	12.9 (6.2–22.3)	10.9 (6.8–16.4)
	Oman	2.7 (0.09–12.5)	7.9 (1.5–25.7)	6.6 (1.7–19.2)
	Palestine	4.2 (0.2–11.5)	12.0 (4.5–24.0)	10.0 (4.9–17.8)
	Yemen	1.5 (0.1–3.9)	4.7 (2.1–9.0)	3.9 (2.3–6.3)
	United Arab Emirates	4.3 (0.3–10.2)	12.4 (5.4–21.7)	10.4 (5.9–15.9)
	Turkey	4.3 (0.3–9.9)	12.4 (6.0–21.0)	10.4 (6.5–15.5)
	Syria	7.4 (0.6–15.8)	19.8 (10.0–31.2)	16.9 (10.9–23.8)
	Lebanon	3.4 (0.2–9.6)	10.0 (3.6–20.4)	8.4 (4.0–15.0)
	Iraq	5.4 (0.3–15.2)	15.2 (5.4–30.3)	12.8 (5.9–23.0)
	Cyprus	4.3 (0.2–12.5)	12.4 (4.5–25.7)	10.4 (4.9–19.2)
	Bahrain	0.3 (0.07–24.2)	1.2 (1.2–43.5)	1.0 (1.3–34.6)
	Jordan	3.1 (0.1–9.5)	9.0 (3.1–20.4)	7.5 (3.3–15.0)
	Egypt	4.0 (0.2–10.9)	11.5 (4.5–22.8)	9.6 (4.9–16.9)
	Iran	4.2 (0.3–9.2)	12.0 (5.7–19.8)	10.0 (6.2–14.5)
Sex	Female	4.7 (0.4–9.9)	13.4 (6.8–21.0)	11.3 (7.4–15.5)
	Male	3.6 (0.3–8.2)	10.5 (5.1–16.7)	8.8 (5.6–13.0)
Total (Middle East)		**4.0 (0.3–9.6)**	**11.5 (5.1–20.4)**	**9.6 (5.6–15.0)**

Hindawi, Journal of Obesity, 2022, Article ID 8074837, https://doi.org/10.1155/2022/8074837

Overall Prevalence of Overweight in Middle East Countries



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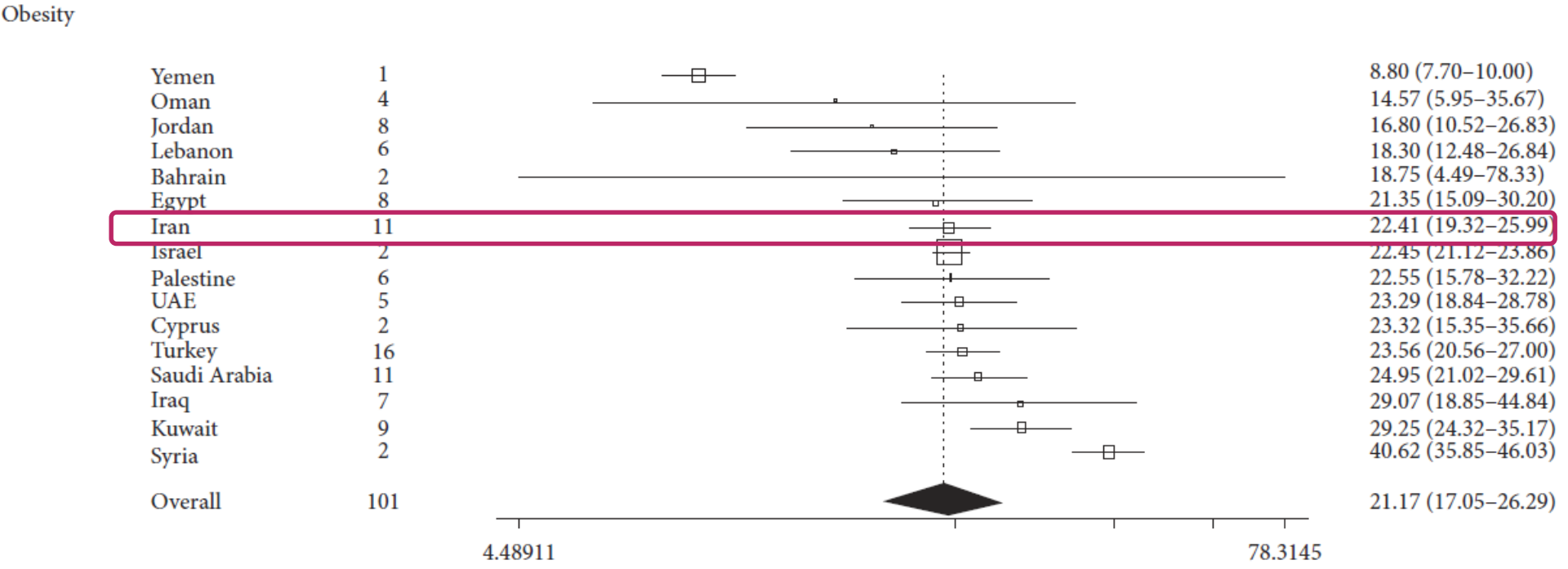
Overall Prevalence of Obesity in Middle East Countries



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Results & Conclusions

- The findings showed that obesity prevalence increased with age so that the highest prevalence of obesity and overweight was observed in people >40 years old.
- Obesity prevalence in the Middle East area remained steady between 2000–2006 and 2014–2020 (23%).
- During these time intervals, the prevalence of overweight decreased from 34.83 (95% CI: 32.40–37.45) to 32.85 (95% CI: 31.39–34.38).
- Therefore, implementing intervention programs to prevent and control obesity and overweight in the Middle East is essential.

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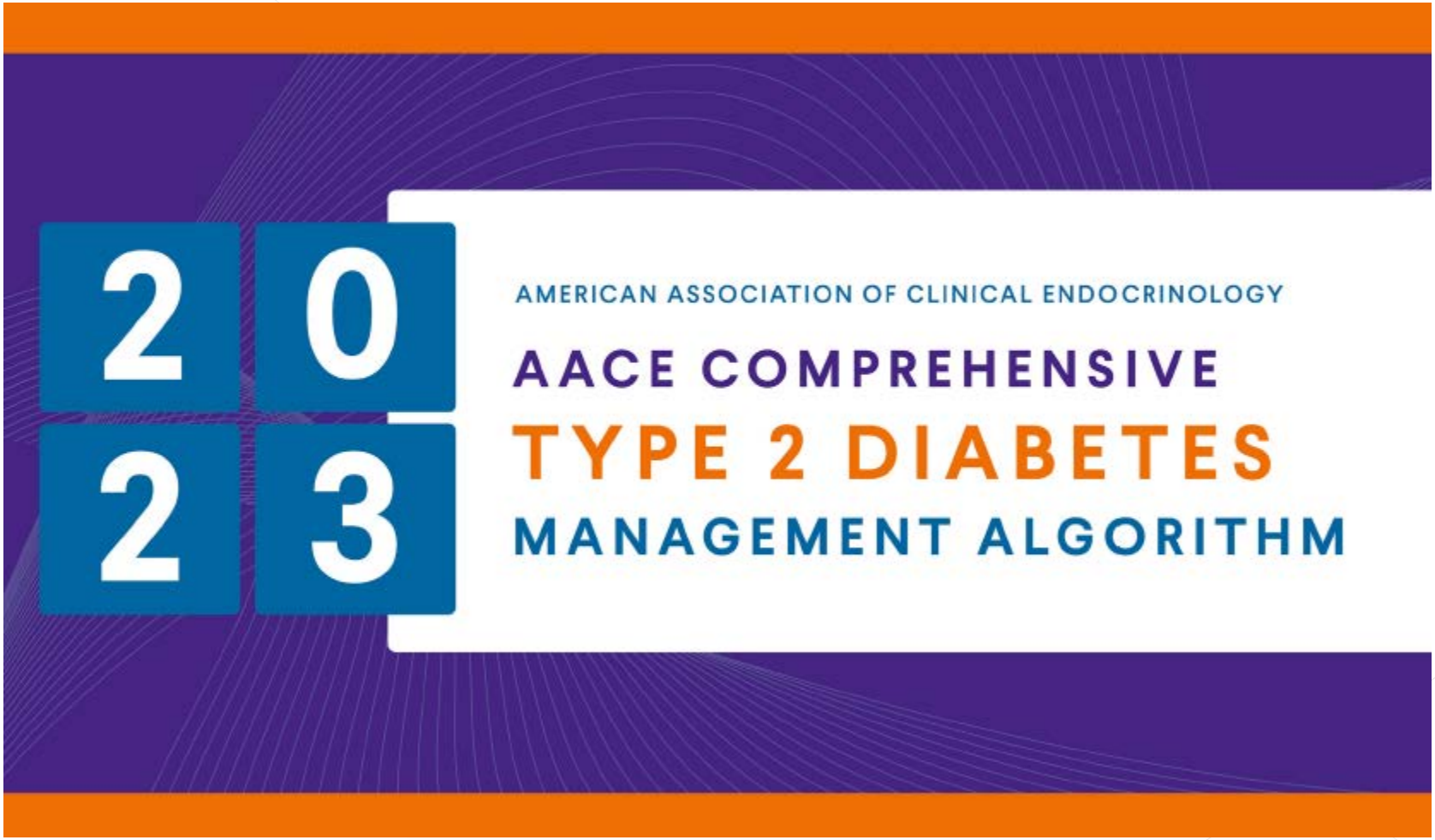
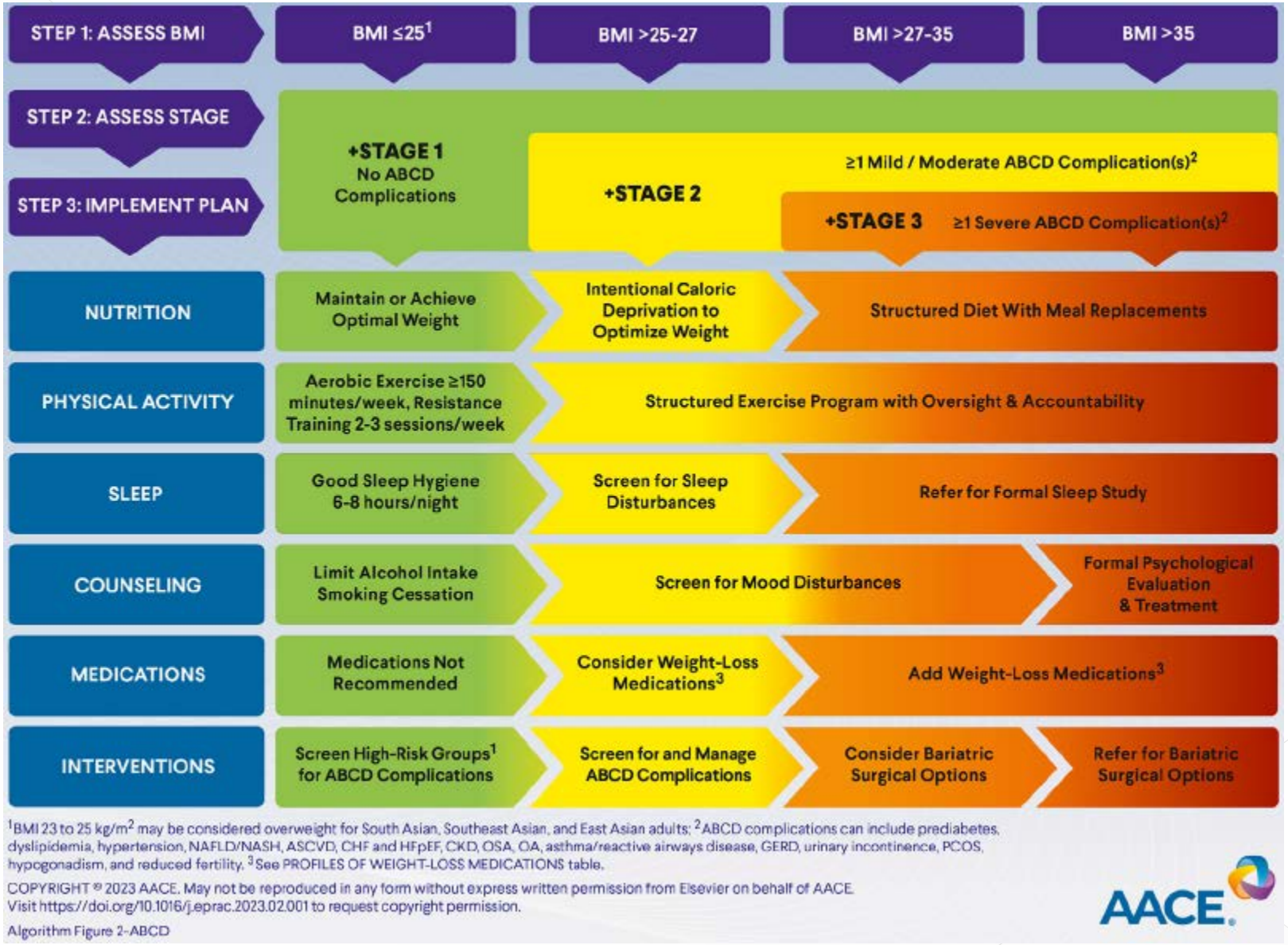
Diagnosis and Medical Management of Adult Patients with Obesity: AACE/ACE Framework



Endocrine Practice 29 (2023) 305e340

Complications-Centric Model for the Care Person with Overweight/Obesity (Adiposity-Based Chronic Disease)



[1]BMI 23 to 25 kg/m^2 may be considered overweight for South Asian, Southeast Asian, and East Asian adults; [2]ABCD complications can include prediabetes, dyslipidemia, hypertension, NAFLD/NASH, ASCVD, CHF and HFpEF, CKD, OSA, OA, asthma/reactive airways disease, GERD, urinary incontinence, PCOS, hypogonadism, and reduced fertility. [3]See PROFILES OF WEIGHT-LOSS MEDICATIONS table.

Algorithm Figure 2-ABCD

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Weight-Loss Medications based on AACE/ACE guideline

	SEMAGLUTIDE	LIRAGLUTIDE	PHENTERMINE/ TOPIRAMATE-ER	NALTREXONE-ER/ BUPROPRION-ER	ORLISTAT	PHENTERMINE[1]
CLASS	GLP-1 RA	GLP-1 RA	Sympathomimetic Amine/Gabaminergic	Opioid-Receptor Antagonist/DA-Norepi Reuptake inhibitor	GI Lipase Inhibitor	Sympathomimetic
WEIGHT LOSS[2]	15%-18%	5%-6%	9%-10%	4%-6%	4%	3%[2]
MECHANISM	Decreased Appetite Delayed Gastric Emptying	Decreased Appetite Delayed Gastric Emptying	Decreased Appetite Increased Satiety	Decreased Cravings Decreased Appetite	Decreased Fat Absorption	Decreased Appetite
DELIVERY	Weekly Subcutaneous Injection	Daily Subcutaneous Injection	Oral	Oral	Oral	Oral
STARTING DOSE	0.25 mg/week	0.6 mg/day	3.75 mg/23 mg daily	8 mg/90 mg daily	120 mg three times daily	15 mg daily
TREATMENT DOSE	2.4 mg/week	3 mg/day	7.5 mg/46 mg daily (maximum 15 mg/92 mg daily)	16 mg/180 mg twice per day	120 mg three times daily	37.5 mg daily[1]
POTENTIAL SIDE EFFECTS	Nausea/Vomiting Diarrhea Constipation Headache Fatigue	Nausea/Vomiting Diarrhea Constipation Headache Fatigue	Restlessness Insomnia Headache Dry Mouth Blurred Vision Tachycardia/BP Elevation Paresthesia Dysgeusia Mental Clouding/Mood Changes	Nausea/Vomiting Diarrhea Constipation Headache Fatigue Insomnia Dry Mouth Blurred Vision Agitation/Mood Changes	Flatulence Fecal Urgency Oily Stools Fat-Soluble Vitamin Drug Malabsorption	Restlessness Insomnia Headache Dry Mouth Tachycardia/BP Elevation
CAUTIONS AND CONTRAINDICATIONS[3]	MTC/MEN2 Tachycardia Pancreatitis/ Gallbladder Disease Diabetic Retinopathy	MTC/MEN2 Tachycardia Pancreatitis/ Gallbladder Disease	Glaucoma Hyperthyroidism Urolithiasis Metabolic Acidosis	Seizure Risk Uncontrolled Hypertension Chronic Opioid Use	Organ Transplant Urolithiasis (Oxalate) Cholestasis	Active CAD Uncontrolled Hypertension Hyperthyroidism Agitated States
ACCESS/COST	$$$	$$$	$$	$$	$$	$

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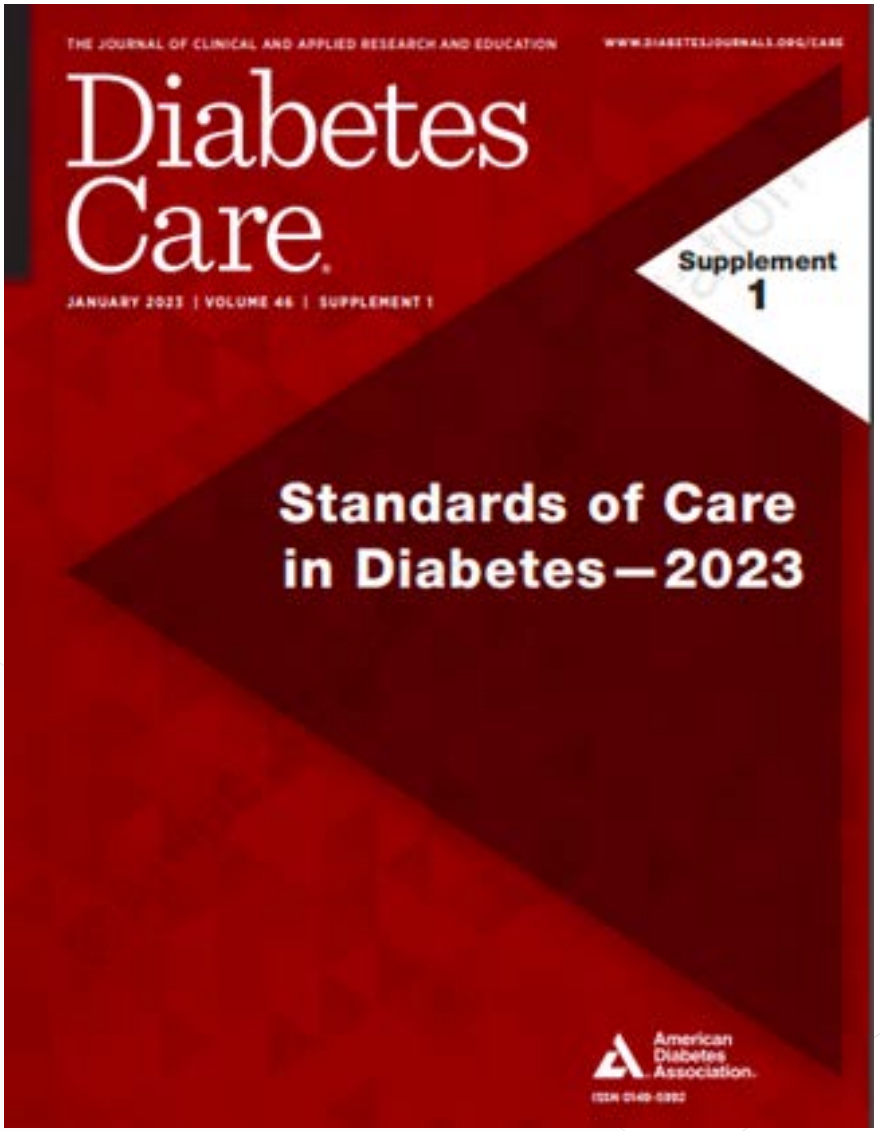
Recommendations of ADA 2023 Guideline

Standard of Medical Care in Diabetes-2023/The American Diabetes Association Guideline



Diabetes Care 2023;46(Suppl. 1):S140–S157.

Healthy Lifestyle behaviors; Diabete

Goal: Cardiorenal Risk Reduction in High-risk Patients with
CV RISK Manager

+ASCVD
Defined differently across CVOTs but all included individuals with established CVD (e.g. MI, stroke any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk
While definitions vary, most comprise≥ 55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia or albuminuria

+ASCVD/INDICATORS OF HIGH RISK

GLP-1 RA with proven CVD benefit — Either/ or — SGLT2i with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit and vice versa
- TZD

If additional cardiorenal risk reduction or glycemic lowering needed

ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

Achievement and Maintenance of Weight Management Goal

Set individualized weight management goals

General lifestyle advice: medical nutrition

Intensive evidence-

Efficacy for weight loss

Very high:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If HbA1C above target

Identify barriers to goals:
- Consider DSMES referral to self-efficacy to achievement of goal
- Consider technology (e.g. diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact on achievement of goals

Medications approved by the FDA for the treatment of overweight or obesity in adults

Medication name	Typical adult maintenance dose	Average wholesale price (30-day supply) (128)	National Average Drug Acquisition Cost (30-day supply) (129)	1-Year (52- or 56-week) mean weight loss (% loss from baseline)		Common side effects (130–134)	Possible safety concerns/ considerations (130–134)
				Treatment arms	Weight loss (% loss from baseline)		
Short-term treatment (≤12 weeks)							
Sympathomimetic amine anorectic							
Phentermine (135)	8–37.5 mg q.d.*	$5–$56 (37.5 mg dose)	$2–$3 (37.5 mg dose)	15 mg q.d.† 7.5 mg q.d.† PBO	6.1 5.5 1.2	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	• Contraindicated for use in combination with monoamine oxidase inhibitors
Long-term treatment (>12 weeks)							
Lipase inhibitor							
Orlistat (4)	60 mg t.i.d. (OTC) 120 mg t.i.d. (Rx)	$41–$82 $781–$904	NA $722	120 mg t.i.d.‡ PBO	9.6 5.6	Abdominal pain, flatulence, fecal urgency	• Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants, etc.) • Rare cases of severe liver injury reported • Cholelithiasis • Nephrolithiasis
Sympathomimetic amine anorectic/antiepileptic combination							
Phentermine/ topiramate ER (45)	7.5 mg/46 mg q.d.§	$223 (7.5 mg/46 mg dose)	$179 (7.5 mg/46 mg dose)	15 mg/92 mg q.d.‖ 7.5 mg/46 mg q.d.‖ PBO	9.8 7.8 1.2	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure	• Contraindicated for use in combination with monoamine oxidase inhibitors • Birth defects • Cognitive impairment
Opioid antagonist/antidepressant combination							
Naltrexone/ bupropion ER (16)	16 mg/180 mg b.i.d.	$750	$599	16 mg/180 mg b.i.d. PBO	5.0 1.8	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	• Acute angle-closure glaucoma • Contraindicated in people with unmanaged hypertension and/or seizure disorders • Contraindicated for use with chronic opioid therapy • Acute angle-closure glaucoma **Black box warning:** • Risk of suicidal behavior/ideation in people younger than 24 years old who have depression

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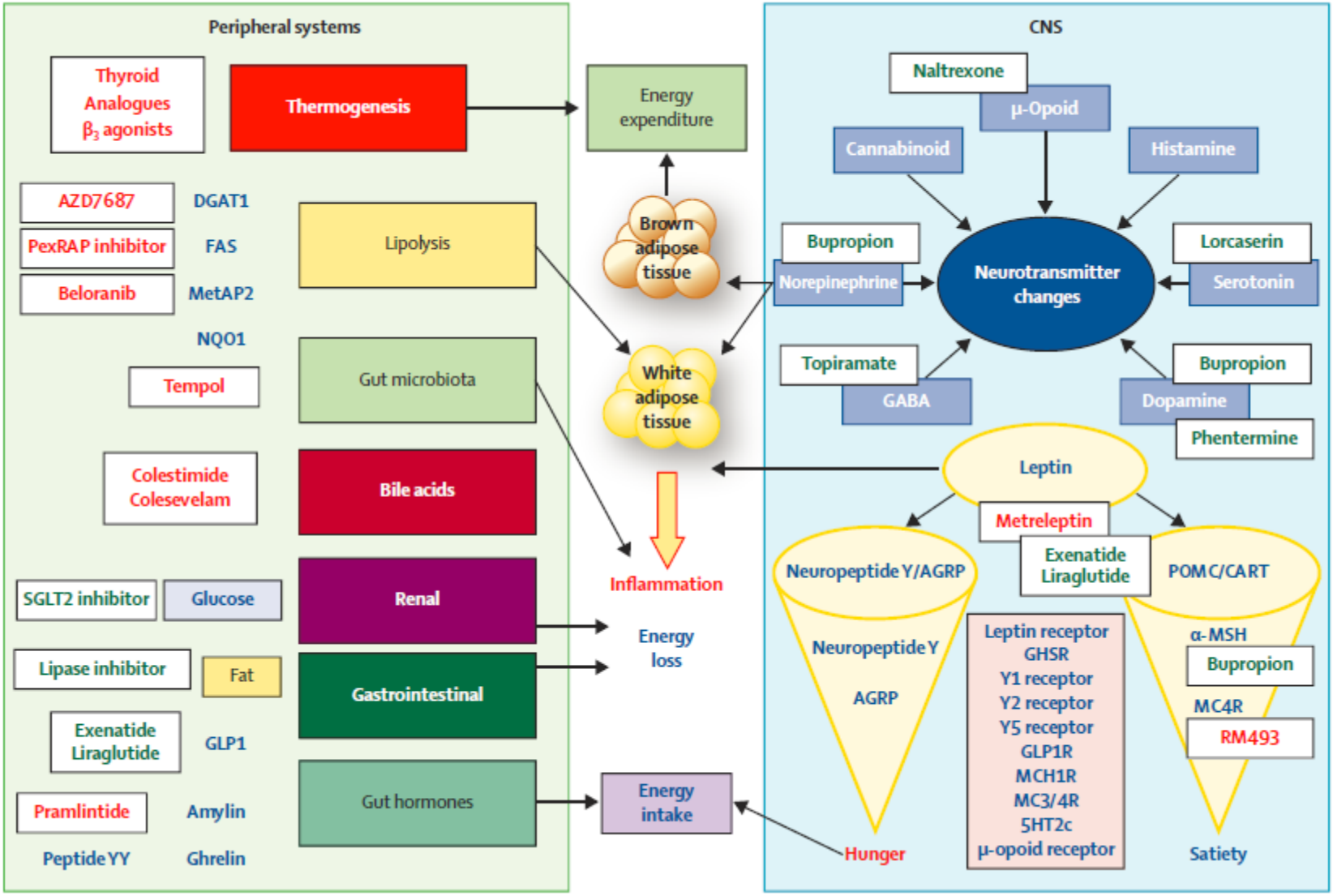
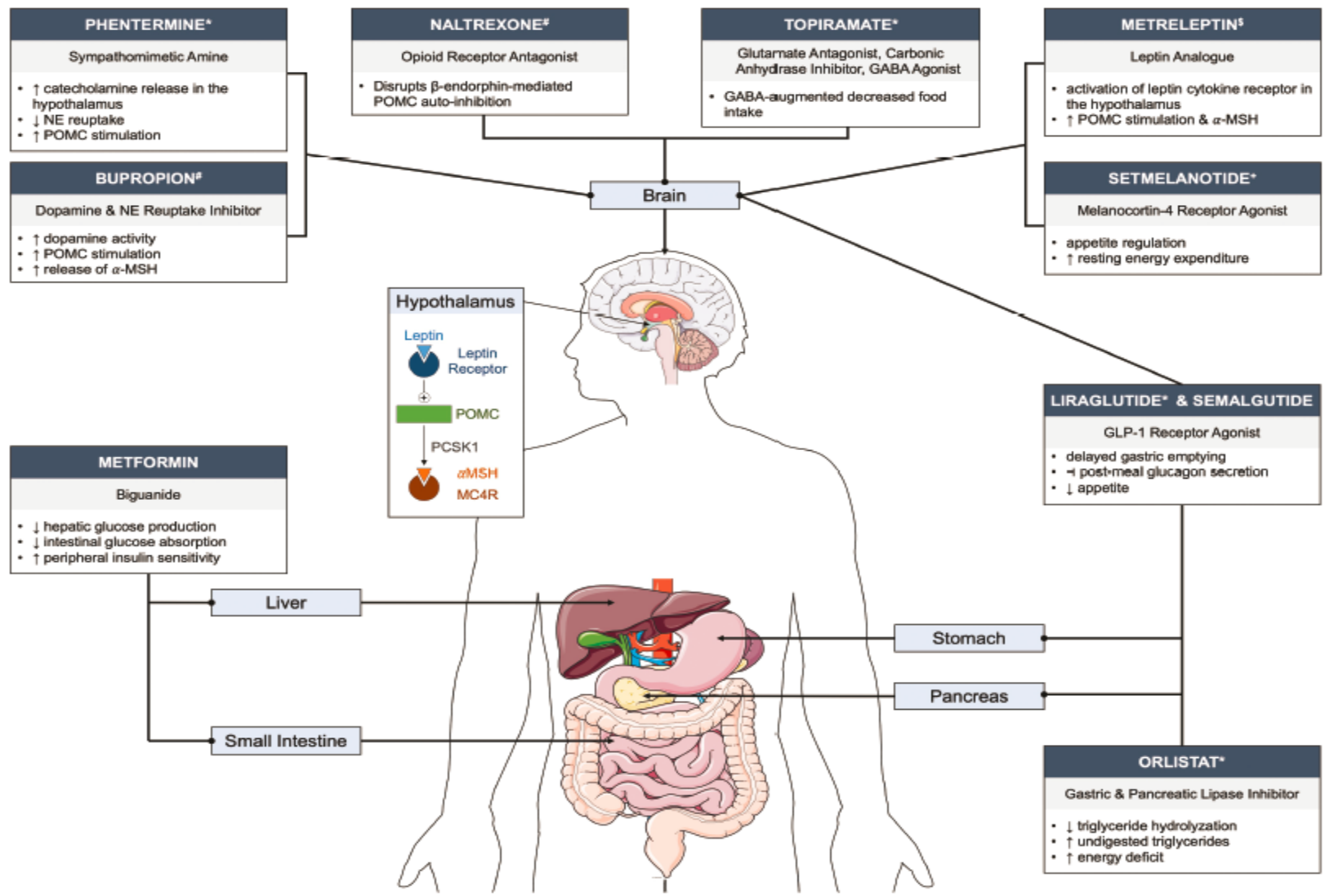
Targets for anti-obesity drugs



Lancet 2016; 387: 1947–56

The sites and mechanisms of actions of medications used in clinical practice for the treatment of obesity



Medications currently used with US Food and Drug Administration approval and off-label for management of adolescent obesity

Drug	FDA-approved indication and age group	Adverse reactions, side effects	Dose	Contraindications, precautions, and black-box warnings
Orlistat	Approved in conjunction with a reduced-calorie diet for pediatric and adult obesity Xenical (120 mg) is approved for ages ≥ 12 y (prescription) Alli (60 mg) is approved for adults aged ≥ 18 (OTC)	Steatorrhea, fecal incontinence, and frequent/urgent bowel movements (common; increased risk when taken with high-fat diet) Reduced absorption of certain fat-soluble vitamins and β-carotene Drug interactions: Can decrease cyclosporine exposure. Monitor patients taking levothyroxine or warfarin concurrently	120 mg by mouth 3 times daily with each main meal containing fat (during or up to 1 h after meal)	Contraindications: pregnancy, patients with chronic malabsorption or cholestasis. Multivitamin that contains fat-soluble vitamins should be taken; rare cases of severe liver injury have been reported; increased risk of cholelithiasis. Increased levels of urinary oxalate. Exercise caution when prescribing orlistat to patients with history of hyperoxaluria or calcium oxalate nephrolithiasis
Topiramate	Not approved for treatment of obesity as monotherapy	Adverse effects tend to increase with higher doses and include paresthesia, hypoesthesia, changes in taste, and psychomotor impairment. Concerns for effects of topiramate on cognition in children have previously been raised	Topiramate dosage for weight loss in adults 64-400 mg daily	Dose titration with 2 wk between increases can reduce adverse effects. Gradual taper when weaning off recommended to reduce risk of precipitating seizures

Medications currently used with US Food and Drug Administration approval and off-label for management of adolescent obesity

Drug	FDA-approved indication and age group	Adverse reactions, side effects	Dose	Contraindications, precautions, and black-box warnings
Phentermine	Short-term (up to 12 wk) adjunct in a regimen of weight reduction based on exercise, behavioral modification, and caloric restriction in management of exogenous obesity for patients with initial BMI ≥ 30 or ≥ 27 in presence of other risk factors (eg, controlled hypertension, diabetes, hyperlipidemia). Not recommended for use in pediatric patients aged ≤ 16 y	Dry mouth, constipation, diarrhea, and insomnia, palpitations, tachycardia, elevated blood pressure, overstimulation, restlessness, dizziness, euphoria, dysphoria, tremor, headache, psychosis, and changes in libido Adverse reactions also include rare cases of primary pulmonary hypertension, ischemic events, and serious regurgitant cardiac valvular disease Drug interactions: monoamine oxidase inhibitors (risk of hypertensive crisis), insulin and oral hypoglycemic medications, adrenergic neuron blocking drugs	15 to 37.5 mg by mouth once daily	Contraindications: pregnancy, nursing, agitated states, patients with cardiovascular disease, hyperthyroidism, glaucoma, history of drug abuse, and during or within 14 d following administration of monoamine oxidase inhibitors Coadministration with other drugs for weight loss not recommended. Tolerance to anorectic effect usually develops within several weeks. Phentermine may impair ability of patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle. Risk of abuse and dependence. Concomitant alcohol use may result in adverse drug reaction Use caution in patients with hypertension. Reduction in dose of insulin or oral hypoglycemic medication may be required in some patients

Medications currently used with US Food and Drug Administration approval and off-label for management of adolescent obesity

Drug	FDA-approved indication and age group	Adverse reactions, side effects	Dose	Contraindications, precautions, and black-box warnings
Phentermine-Topiramate	Approved as adjunct to reduced calorie diet and increased physical activity for chronic weight management in adults with BMI ≥ 30 kg/m^2, or ≥ 27 kg/m^2 in the presence of other risk factors and children 12 years old and older with BMI >95%ile for age and sex.	Common side effects: paresthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth. Drug interactions: oral contraceptives, non–potassium-sparing diuretics. May potentiate effects of alcohol	Once daily by mouth in the morning. Dose combinations (phentermine/topiramate): 3.75/23 mg, 7.5/46 mg, 11.25/69 mg, and 15/92 mg. Start at lowest dose for 2 wk, then increase to next higher dose. If < 3% weight loss at 12 wk, increase to next higher dose for 2 wk and then increase to maximum dose (discontinue if < 5% weight loss after 12 wk at highest dose)	Contraindications: Pregnancy, glaucoma, hyperthyroidism and during to within 14 d of taking monoamine inhibitors. Nursing mothers: discontinue drug or nursing Warnings and precautions: fetal toxicity (oral clefts) - recommend pregnancy testing prior to initiation and monthly during treatment and use of effective contraception; increased heart rate; suicidal behavior and ideation; mood or sleep disorders; cognitive impairment. In pediatric patients can cause slowing of linear growth. Discontinue if suicidal behavior/ideation; acute myopia and secondary angle-closure glaucoma. Gradual taper when weaning off is recommended to reduce risk of precipitating seizures. Use caution with metabolic acidosis, elevated creatinine. Weight loss

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Metformin	Approved as adjunct to diet and exercise for patients with type 2 diabetes mellitus in patients age ≥ 10 years. Used off-label for pediatric obesity and treatment of polycystic ovarian syndrome	Most common side effects: diarrhea, nausea/vomiting, flatulence, hypoglycemia with concomitant use of other glucose-lowering drugs. Most serious side effect: lactic acidosis (rare) Vitamin B_{12} deficiency can also occur. Stop metformin before surgery or when undergoing radiologic studies with intravenous iodinated contrast	Dose ranges from 250 mg orally, twice daily, before meals titrating up to 500 mg twice daily to maximum dose of 1000 mg twice daily	Black-box warning: Lactic acidosis —risk factors include renal impairment, hepatic impairment, concomitant use of certain drugs (eg, carbonic anhydrase inhibitors such as topiramate), intravascular iodinated contrast agents, hypoxic states Contraindicated in diabetic ketoacidosis and severe renal impairment (eGFR < 30 mL/min/1.73 m^2) Potential interactions with glyburide, furosemide, nifedipine, and drugs that reduce metformin clearance

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Naltrexone-Bupropion	Approved as adjunct to reduced calorie diet and increased physical activity for adults with BMI ≥ 30 or ≥ 27 in presence of other risk factors. Used off-label for pediatric obesity	Headache, nausea, vomiting, constipation, dry mouth, insomnia, and agitation	Extended-release tablets containing 8 mg naltrexone/90 mg bupropion. Starting dose 1 tablet by mouth once daily, increasing weekly by 1 tablet over 4 wk to 2 tablets twice daily.	Black-box warnings: (1) Increased risk of suicidal thinking and behavior in children, adolescents and young adults. (2) Serious neuropsychiatric events have been reported in patients taking bupropion for smoking cessation. Contraindications: uncontrolled hypertension, seizure disorders, anorexia nervosa or bulimia, undergoing abrupt discontinuation of alcohol, benzodiazepines, chronic opioid use, during or within 14 d of taking monoamine oxidase inhibitors. Nursing mothers: discontinue drug or nursing Warnings and precautions: risk of increased blood pressure and heart rate; hepatotoxicity, angle closure glaucoma. Weight loss may cause hypoglycemia in patients taking antidiabetic agents

Key Message for Healthcare Providers

- Pharmacological treatments are an effective and scalable approach to treating obesity. As with any chronic disease, such as type 2 diabetes (T2DM) or hypertension, pharmacotherapy is an important pillar in the management of obesity.

- The focus of obesity management should be the improvement of health parameters (metabolic, mechanical, mental, and/or quality of life [QoL]), not solely weight reduction, and should include outcomes that the patient identifies as important. Obesity is defined by body mass index (BMI) in clinical trials, which itself does not adequately reflect the burden of adiposity-related disease.

Key Message for Healthcare Providers

- There are four medications indicated for long-term obesity management as adjuncts to health-behaviour changes, All four medications are effective in producing clinically significant weight loss and health benefits greater than placebo over a duration of at least one year.

- The individual response to pharmacotherapy for obesity management is heterogeneous. Efficacy (both for weight and management of obesity-related health issues), mechanism of action, safety, potential side effects/tolerability, contraindications, medication interactions, mode of administration and cost are important considerations in choosing the most appropriate obesity pharmacotherapy.

Key Message for Healthcare Providers

- Obesity medications are intended as part of a long-term treatment strategy. Clinical trials of pharmacotherapy for obesity management consistently demonstrate regain of weight when treatment is stopped.

- Medications that are not approved as pharmacotherapy for obesity management should not be used for this purpose.

Thank you for your attention