AACE/ACE ALGORITHM FOR THE MEDICAL CARE OF PATIENTS WITH OBESITY

Patient Presentation	Screen positive for overweight or obesity BMI ≥25 kg/m² (≥23 kg/m² in some ethnicities)	Presence of weight-related disease or complication that could be improved by weight loss therapy

Diagnosis

Evaluation

- Medical history • Physical examination • Clinical laboratory
- Review of systems, emphasizing weight related complications
- Obesity history: graph weight vs age, lifestyle patterns/preferences, previous interventions

Anthropometric Diagnosis

- Confirm that elevated BMI represents excess adiposity
- Measure waist circumference to evaluate cardiometabolic disease risk

BMI kg/m²

Clinical Diagnosis

<25 NORMAL WEIGHT <23 in certain ethnicities Waist circumference below regional/ethnic cutoffs	25–29.9 OVERWEIGHT | ≥30 OBESITY **Checklist of Obesity-Related Complications** (staging and risk stratification based on complication-specific criteria)		
	None	**Mild to Moderate**	**Severe**

Diagnostic Categories	**NORMAL WEIGHT (no obesity)**	**STAGE 0**	**STAGE 1**	**STAGE 2**
		No complications	One or more mild-to-moderate complications or may be treated effectively with moderate weight loss	At least one severe complication or requires more aggressive weight loss for effective treatment
		OVERWEIGHT **BMI 25–29.9** OBESITY **BMI ≥30**	**BMI ≥25**	**BMI ≥25**
Phases of Chronic Disease Prevention and Treatment Goals	**PRIMARY** Prevent overweight/obesity	**SECONDARY** Prevent progressive weight gain or achieve weight loss to prevent complications	**TERTIARY** Achieve weight loss sufficient to ameliorate the complications and prevent further deterioration	
Treatment Based on Clinical Judgment	• Healthy meal plan • Physical activity • Health education • Built environment	• Lifestyle/behavioral therapy • Consider pharmacotherapy if lifestyle alone not effective	• Lifestyle/behavioral therapy • Consider pharmacotherapy (BMI ≥27)	• Lifestyle/behavioral therapy • Add pharmacotherapy (BMI ≥27) • Consider bariatric surgery (BMI ≥35)

Follow-Up	• Once the plateau for weight loss has been achieved, re-evaluate the weight-related complications. If the complications have not been treated to target, then weight loss therapy should be intensified or complication-specific interventions need to be employed. • Obesity is a chronic disease and the diagnostic categories for obesity may not be static. Therefore, patients require ongoing follow-up, re-evaluation, and long-term treatment.

Abbreviation: BMI = body mass index

ANTHROPOMETRIC COMPONENT OF THE MEDICAL DIAGNOSIS OF OBESITY

Evidence-based screening and diagnosis for excess adiposity in clinical settings

Screening → **Annual BMI**

- BMI ≥25 kg/m^2
- BMI ≥23 kg/m^2 for some ethnicities

→ **Diagnosis (Anthropometric Component)**

- BMI <25 kg/m^2
- BMI <23 kg/m^2 for some ethnicities

1. **Clinical interpretation of BMI:** Ensure elevated BMI is indicative of excess adiposity by assessing: age, gender, muscularity, hydration status, edema, third space fluid collection, large tumors, sarcopenia
2. **Waist circumference if BMI <35:** Adds information pertaining to cardiometabolic disease risk; use gender- and ethnicity-specific cut-off values
3. **Can consider body composition technologies:** eg, bioelectrical impedance, air/water displacement plethysmography, or dual-energy x-ray absorptiometry scan

→ **Clinical Component of Diagnosis**

Abbreviation: BMI = body mass index.

CLINICAL COMPONENT OF THE MEDICAL DIAGNOSIS OF OBESITY

Evaluate for a checklist of weight-related complications. Candidates for weight-loss therapy can present with either excess adiposity (ie, the anthropometric component) or weight-related complications (ie, the clinical component)

Patients Present with Overweight or Obesity (Anthropometric Component)	Candidates for Weight Loss Therapy	Patients Present with Weight-Related Disease or Complication (Clinical Component)
Patients present with BMI ≥25 kg/m^2, or ≥23 kg/m^2 in certain ethnicities, and excess adiposity	Evaluate for weight-related complications → / Evaluate for overweight or obesity ←	Prediabetes
		Metabolic Syndrome
		Type 2 Diabetes
		Dyslipidemia
		Hypertension
		Cardiovascular Disease
		Nonalcoholic Fatty Liver Disease
		Polycystic Ovary Syndrome
		Female Infertility
		Male Hypogonadism
		Obstructive Sleep Apnea
		Asthma/Reactive Airway Disease
		Osteoarthritis
		Urinary Stress Incontinence
		Gastroesophageal Reflux Disease
		Depression

CHECKLIST OF WEIGHT-RELATED COMPLICATIONS: SCREENING AND DIAGNOSES IN PATIENTS WITH OVERWEIGHT/OBESITY

Weight-Related Complication	Basis for Screening and/or Diagnosis	Suggested Secondary Testing When Needed To Confirm Diagnosis, Stage Severity, or Guide Therapy
Prediabetes	Fasting glucose; A1C; 2-hour OGTT glucose	If fasting glucose is 100-125 mg/dL, a repeat elevated fasting glucose completes diagnosis of IFG; however, 2-hour OGTT should also be performed to exclude diabetes and IGT. Fasting and 2-hour OGTT should be performed if initial fasting glucose is normal and A1C is elevated, or in high-risk patients based on family history or metabolic syndrome.
Metabolic Syndrome	Waist circumference, blood pressure, fasting glucose, triglycerides, HDL-c	Initial evaluation completes diagnosis; OGTT to test for IGT or diabetes.
Type 2 Diabetes	Fasting glucose; A1C; 2-hour OGTT glucose; symptoms of hyperglycemia	Overtly elevated (i.e., ≥200 mg/dL) or a repeat fasting glucose ≥126 mg/dL completes diagnosis. If fasting glucose and/or A1C is consistent with prediabetes, 2-hour OGTT should be performed to test for diabetes. A1C should be performed to help guide therapy.
Dyslipidemia	Lipid panel (total cholesterol, HDL-c, triglycerides, LDL-c, non-HDL-c)	Lipid panel completes diagnosis; lipoprotein subclasses, Apo B-100 may further define risk.
Hypertension	Sitting blood pressure	Repeat elevated blood pressure measurements to complete diagnosis; home blood pressure or ambulatory blood pressure monitoring may help complete testing.
Cardiovascular Disease	Physical exam; ROS; history and medical records	Additional testing based on findings and risk status (eg, ankle-brachial index, stress testing, coronary artery calcium score and the MESA risk score calculator, arteriography, carotid ultrasound)
NAFLD/NASH	Physical exam; LFTs	Imaging (eg, ultrasound, MRI, elastography) and/or liver biopsy needed to complete diagnosis.
PCOS and Female Infertility	Physical exam; ROS; menstrual and reproductive history	Hormonal testing (eg, androgen levels, SHBG, LH/FSH, estradiol), ovulation testing, imaging of ovaries, may be needed to complete diagnosis.
Male Hypogonadism	Physical exam; ROS	Hormonal testing (total and free testosterone, SHBG, LH/FSH, prolactin) as needed to complete diagnosis.
Obstructive Sleep Apnea	Physical exam; neck circumference; ROS	Polysomnography needed to complete diagnosis.
Asthma / Respiratory Disease	Physical exam; ROS	Chest x-ray and spirometry study may be needed to complete diagnosis.
Osteoarthritis	Physical exam; ROS	Radiographic imaging may be needed to complete diagnosis.
Urinary Stress Incontinence	Physical exam; ROS	Urine culture, urodynamic testing may be needed to complete diagnosis.
GERD	Physical exam; ROS	Endoscopy, esophageal motility study may be needed to complete diagnosis.
Depression, Anxiety, Binge Eating Disorder, Stigmatization	History; ROS	Screening/diagnostic evaluation or questionnaires based on criteria in Diagnostic and Statistical Manual of Mental Disorders; referral to clinical psychologist or psychiatrist.
Disability	Physical exam; ROS	Functional testing may be helpful.
Additional Evaluation Relevant to the Differential Diagnosis of Obesity		
Interpretation of BMI	Physical exam to ensure that BMI value is indicative of excess adiposity	Assess muscularity, edema, volume status, pregnancy, third space fluid accumulation, sarcopenia, large tumors, lipodystrohy, etc. Bioelectric impedance, air/water displacement plethysmography, or dual-energy absorptiometry scan may be considered.
Obesity Secondary to Hormonal Disorder	Physical exam; ROS	TSH for suspected hypothyroidism; salivary/serum/urine cortisol for hypercortisolism if clinical findings or symptoms present.
Iatrogenic Obesity (e.g., secondary to medications)	Review current medications and medication history	Follow-up following withdrawal of offending medication and/or substitution with weight-neutral alternative may be needed to complete diagnosis.
Genetic Syndrome	Physical exam; ROS; family history	If clinical findings are suggestive, genetic testing of patient and perhaps family members may be needed to complete diagnosis.

Abbreviations: A1C = glycated hemoglobin; BMI = body mass index; FSH = follicle-stimulating hormone; GERD = gastroesophageal reflux disease; HDL-c = high-density lipoprotein cholesterol; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; LFTs = liver function tests; LDL-c = low-density lipoprotein cholesterol; LH = luteinizing hormone; MRI = magnetic resonance imaging; NAFLD = non-alcoholic fatty liver disease; NASH = non-alcoholic steatohepatitis; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; ROS = review of symptoms; SHBG = sex hormone binding globulin; TSH = thyroid-stimulating hormone.

LIFESTYLE THERAPY

Evidence-based lifestyle therapy for treatment of obesity should include three components

MEAL PLAN

- Reduced-calorie healthy meal plan
- ~500–750 kcal daily deficit
- Individualize based on personal and cultural preferences
- Meal plans can include: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian
- Meal replacements
- Very low-calorie diet is an option in selected patients and requires medical supervision

Team member or expertise:
dietitian, health educator

PHYSICAL ACTIVITY

- Voluntary aerobic physical activity progressing to >150 minutes/week performed on 3–5 separate days per week
- Resistance exercise: single-set repetitions involving major muscle groups, 2–3 times per week
- Reduce sedentary behavior
- Individualize program based on preferences and take into account physical limitations

Team member or expertise:
exercise trainer, physical activity coach, physical/occupational therapist

BEHAVIOR

An interventional package that includes any number of the following:

- Self-monitoring (food intake, exercise, weight)
- Goal setting
- Education (face-to-face meetings, group sessions, remote technologies)
- Problem-solving strategies
- Stimulus control
- Behavioral contracting
- Stress reduction
- Psychological evaluation, counseling, and treatment when needed
- Cognitive restructuring
- Motivational interviewing
- Mobilization of social support structures

Team member or expertise:
health educator, behaviorist, clinical psychologist, psychiatrist

WHEN TO INITIATE WEIGHT-LOSS MEDICATIONS IN PATIENTS WITH OVERWEIGHT/OBESITY

INITIATE LIFESTYLE THERAPY

1. No Complications.
Patients with overweight or obesity who have no clinically significant weight-related complications (secondary prevention)

2. Mild to Moderate Complications.
- Patient with mild to moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to ameliorate the complication (tertiary prevention)
- Note: weight loss medications may also be indicated based on clinical judgment

INITIATE WEIGHT LOSS MEDICATION AS AN ADJUNCT TO LIFESTYLE THERAPY

1. Failure on Lifestyle Therapy.
Add medication for patients who have progressive weight gain or who have not achieved clinical improvement in weight-related complications on lifestyle therapy alone.

2. Weight Regain on Lifestyle Therapy.
Add medication for patients with overweight (BMI 27–29.9 kg/m^2) or obesity who are experiencing weight regain following initial success on lifestyle therapy alone.

3. Presence of Weight-Related Complications.
Initiate medication concurrent with lifestyle therapy for patients with overweight (BMI 27–29.9 kg/m^2) or obesity who have weight-related complications, particularly if severe, in order to achieve sufficient weight loss to ameliorate the complication (tertiary prevention).

TREATMENT GOALS BASED ON DIAGNOSIS IN THE MEDICAL MANAGEMENT OF PATIENTS WITH OBESITY

	DIAGNOSIS		TREATMENT GOALS	
	Anthropometric Component	**Clinical Component**	**Intervention/ Weight-Loss Goal**	**Clinical Goals**
PRIMARY PREVENTION				
Primordial Prevention	BMI ≤25 (≤23 in certain ethnicities)	Obesogenic environment	• Public education • Built environment • Access to healthy foods	Decreased incidence of overweight/obesity in populations
Primary Prevention	BMI ≤25 (≤23 in certain ethnicities)	High-risk individuals or subgroups based on individual or cultural behaviors, ethnicity, family history, biomarkers, or genetics	• Annual BMI screening • Healthy meal plan • Increased physical activity	Decreased incidence of overweight/obesity in high-risk individuals or identifiable subgroups
SECONDARY PREVENTION				
Overweight	BMI 25–29.9 (BMI 23–24.9 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Prevent progressive weight gain or • Weight loss	• Prevent progression to obesity • Prevent the development of weight-related complications
Obesity	BMI ≥30 (≥25 in certain ethnicities)	No clinically significant or detectable weight-related complications	• Weight loss or • Prevent progressive weight gain	Prevent the development of weight-related complications
TERTIARY PREVENTION				
Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome	10%	Prevention of T2DM
		Prediabetes	10%	Prevention of T2DM
		T2DM	5% to ≥15%	• Reduction in A1C • Reduction in number and/or doses of glucose lowering medications • Diabetes remission especially when diabetes duration is short
		Dyslipidemia	5% to ≥15%	• Lower triglycerides • Raise HDL-c • Lower non-HDL-c
		Hypertension	5% to ≥15%	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications
		Nonalcoholic fatty liver disease: Steatosis	5% or more	Reduction in intrahepatocellular lipid
		Nonalcoholic fatty liver disease: Steatohepatitis	10% to 40%	Reduction in inflammation and fibrosis
		Polycystic ovary syndrome	5% to 15% or more	• Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels
		Female infertility	10% or more	• Ovulation • Pregnancy and live birth
		Male hypogonadism	5% to 10% or more	Increase in serum testosterone
		Obstructive sleep apnea	7% to 11% or more	• Improved symptomatology • Decreased apnea-hypopnea index
		Asthma/reactive airway disease	7% to 8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology
		Osteoarthritis	• ≥10% • 5% to 10% or more when coupled with exercise	• Improvement in symptomatology • Increased function
		Urinary stress incontinence	5% to 10% or more	Reduced frequency of incontinence episodes
		Gastroesophageal reflux disease	10% or more	Reduced symptom frequency and severity
		Depression	Uncertain	• Reduction in depression symptomatology • Improvement in depression scores

Abbreviations: A1C = hemoglobin A1c; BMI = body mass index; BP = blood pressure; HDL-c = high-density lipoprotein cholesterol; T2DM = type 2 diabetes mellitus.

PREFERRED WEIGHT-LOSS MEDICATIONS: INDIVIDUALIZATION OF THERAPY

KEY: PREFERRED DRUG | USE WITH CAUTION | AVOID

CLINICAL CHARACTERISTICS OR COEXISTING DISEASES		MEDICATIONS FOR CHRONIC WEIGHT MANAGEMENT				
		Orlistat	**Lorcaserin**	**Phentermine/ topiramate ER**	**Naltrexone ER/ bupropion ER**	**Liraglutide 3 mg**
Diabetes Prevention (metabolic syndrome, prediabetes)			Insufficient data for T2DM prevention		Insufficient data for T2DM prevention	
Type 2 Diabetes Mellitus						
Hypertension				Monitor heart rate	Monitor BP and heart rate. Contraindicated in uncontrolled HTN	Monitor heart rate
Cardiovascular Disease	**CAD**			Monitor heart rate	Monitor heart rate, BP	Monitor heart rate
	Arrhythmia		Monitor for bradycardia	Monitor heart rate, rhythm	Monitor heart rate, rhythm, BP	Monitor heart rate, rhythm
	CHF	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Chronic Kidney Disease	**Mild (50–79 mL/min)**					
	Moderate (30–49 mL/min)			Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg bid	
	Severe (<30 mL/min)	Watch for oxalate nephropathy	Urinary clearance of drug metabolites	Urinary clearance of drug	Urinary clearance of drug	Avoid vomiting and volume depletion
Nephrolithiasis		Calcium oxalate stones		Calcium phosphate stones		
Hepatic Impairment	**Mild-Moderate (Child-Pugh 5–9)**	Watch for cholelithiasis	Hepatic metabolism of drug	Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg in AM	Watch for cholelithiasis
	Severe (Child-Pugh >9)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Depression			Insufficient safety data Avoid combinations of serotonergic drugs	Avoid maximum dose: 15 mg/92 mg per day	Insufficient safety data Avoid in adolescents and young adults	
Anxiety				Avoid max dose: 15 mg/92 mg per day		
Psychoses		Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Binge Eating Disorder			Insufficient data. Possible benefit based on reduction in food cravings	Insufficient data. Possible benefit based on studies with topiramate	Insufficient data. Possible benefit based on studies with bupropion Avoid in patients with purging or bulimia nervosa	Insufficient data
Glaucoma				Contraindicated, may trigger angle closure	May trigger angle closure	
Seizure Disorder				If discontinue at dose of 15 mg/92 mg, taper slowly	Bupropion lowers seizure threshold	
Pancreatitis		Monitor for symptoms				Monitor for symptoms Avoid if prior or current disease
Opioid Use					Will antagonize opioids and opiates	
Women of Reproductive Potential	**Pregnancy**	Use contraception and discontinue orlistat should pregnancy occur	Use contraception and discontinue lorcaserin should pregnancy occur	Use contraception and discontinue phentermine/topiramate should pregnancy occur (perform monthly pregnacy checks to identify early pregnancy)	Use contraception and discontinue naltrexone ER/bupropion ER should pregnancy occur	Use contraception and discontinue liraglutide 3mg should pregnancy occur
	Breast-feeding	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Age ≥65 years *		Limited data available	Insufficient data	Limited data available	Insufficient data	Limited data available
Alcoholism/ Addiction			Might have abuse potential due to euphoria at high doses	Insufficient data. Topiramate might exert therapeutic benefits	Avoid due to seizure risk and lower seizure threshold on bupropion	
Post-Bariatric Surgery		Insufficient data	Insufficient data	Limited data available	Insufficient data	Data available at 1.8 – 3.0 mg/day

* Use medications only with clear health-related goals in mind; assess patient for osteoporosis and sarcopenia.

Abbreviations: BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; HTN = hypertension; T2DM = Type 2 Diabetes Mellitus.

DIAGNOSIS AND MEDICAL MANAGEMENT OF OBESITY

DIAGNOSIS		COMPLICATION-SPECIFIC STAGING AND TREATMENT		
Anthropometric Component (BMI kg/m²)	**Clinical Component**	**Disease Stage**	**Chronic Disease Phase of Prevention**	**Suggested Therapy (based on clinical judgment)**
<25 <23 in certain ethnicities waist circumference below regional/ ethnic cutoffs		**Normal weight** (no obesity)	**Primary**	• **Healthy lifestyle:** healthy meal plan/ physical activity
25–29.9 23–24.9 in certain ethnicities	Evaluate for presence or absence of adiposity-related complications and severity of complications • Metabolic syndrome • Prediabetes • Type 2 diabetes • Dyslipidemia • Hypertension • Cardiovascular disease • Nonalcoholic fatty liver disease • Polycystic ovary syndrome • Female infertility • Male hypogonadism • Obstructive sleep apnea • Asthma/reactive airway disease • Osteoarthritis • Urinary stress incontinence • Gastroesophageal reflux disease • Depression	**Overweight stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions
≥30 ≥25 in certain ethnicities		**Obesity stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to prevent progressive weight gain. (BMI ≥27)
≥25 ≥23 in certain ethnicities		**Obesity stage 1** (1 or more mild-moderate complications)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to achieve therapeutic target or initiate concurrent with lifestyle therapy. (BMI ≥27)
≥25 ≥23 in certain ethnicities		**Obesity stage 2** (at least 1 severe complication)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Add weight-loss medication:** Initiate concurrent with lifestyle therapy. (BMI ≥27) • **Consider bariatric surgery:** (BMI ≥35)

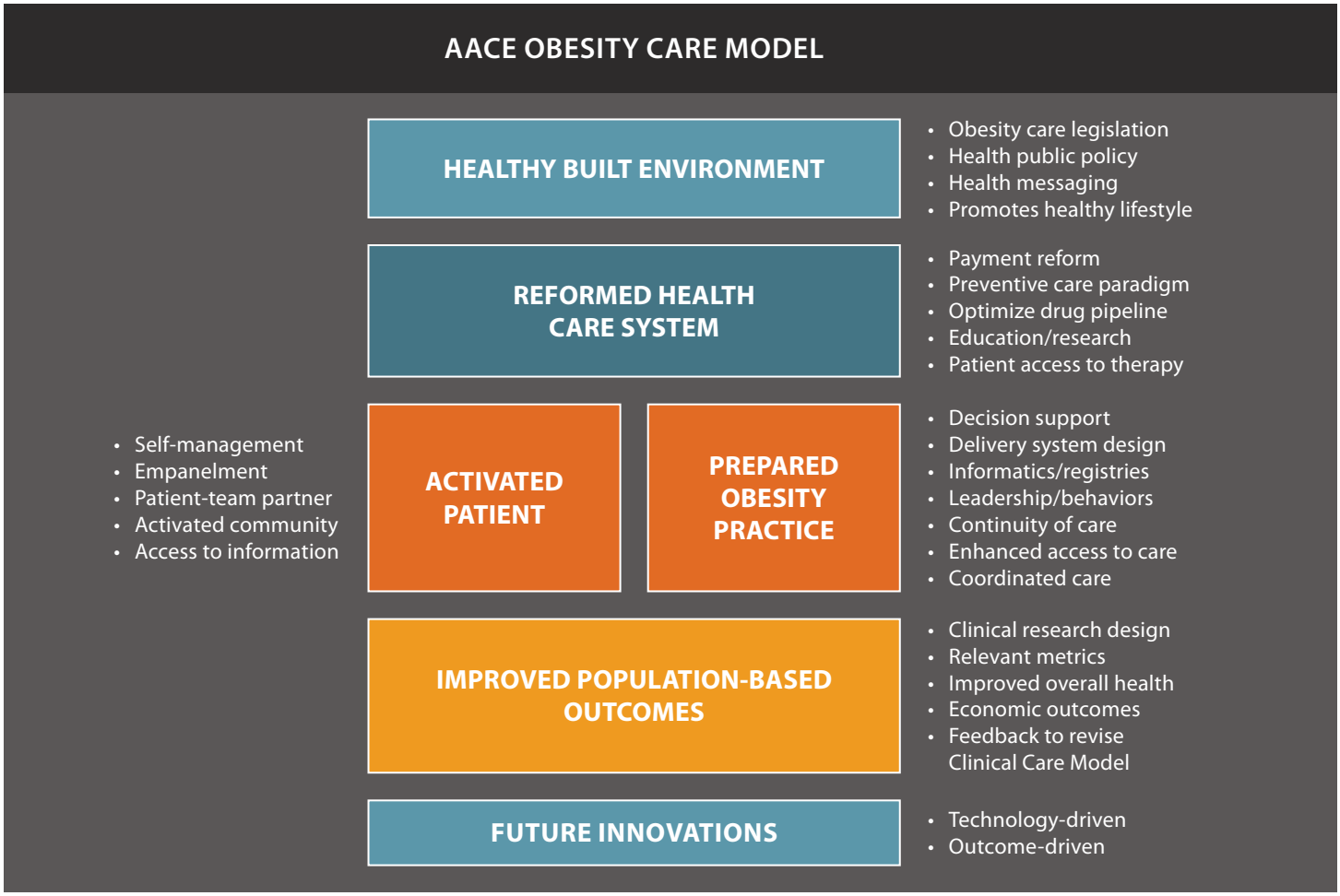
a. All patients with BMI ≥25 have either overweight stage 0, obesity stage 0, obesity stage 1, or obesity stage 2, depending on the initial clinical evaluation for presence and severity of complications. These patients should be followed over time and evaluated for changes in both anthropometric and clinical diagnostic components. The diagnoses of overweight/obesity stage 0, obesity stage 1, and obesity stage 2 are not static, and disease progression may warrant more aggressive weight-loss therapy in the future. BMI values ≥25 have been clinically confirmed to represent excess adiposity after evaluation for muscularity, edema, sarcopenia, etc.

b. Stages are determined using criteria specific to each obesity-related complication; stage 0 = no complication; stage 1 = mild-to-moderate; stage 2 = severe.

c. Treatment plans should be individualized; suggested interventions are appropriate for obtaining the sufficient degree of weight loss generally required to treat the obesity-related complication(s) at the specified stage of severity.

d. BMI ≥27 is consistent with the prescribing information mandated by the US Food and Drug Administration for weight-loss medications.

Abbreviation: BMI = body mass index.



WEIGHT-LOSS MEDICATIONS APPROVED BY THE FDA FOR LONG-TERM TREATMENT OF OBESITY

Anti-obesity Medication (Trade Name) Year of FDA Approval	Mechanism of Action, Study Name, Study Duration: % TBWL Greater Than Placebo	Dose	Common Side Effects	Contraindications, Cautions, and Safety Concerns ✓ Contraindication • Warning, Safety Concern	Monitoring and Comments

Orlistat
 	
(Xenical™)
(Alli™) – OTC
 	
1999
	Lipase inhibitor
	
	XENDOS
	
	1 yr: 4.0%
	4 yr: 2.6%
		120 mg PO TID (before meals)
		
		OTC: 60 mg PO TID (before meals)
			• Steatorrhea
			• Fecal urgency
			• Incontinence
			• Flatulence
			• Oily spotting
			• Frequent bowel movements
			• Abdominal pain
			• Headache
				✓ Pregnancy and breastfeeding
				✓ Chronic malabsorption syndrome
				✓ Cholestasis
				✓ Oxalate nephrolithiasis
				• Rare severe liver injury
				• Cholelithiasis
				• Malabsorption of fat-soluble vitamins
				• Effects on other medications:
				  • Warfarin (enhance)
				  • Antiepileptics (decrease)
				  • Levothyroxine (decrease)
				  • Cyclosporine (decrease)
					Monitor for:
					• Cholelithiasis
					• Nephrolithiasis
					
					- Recommend standard multivitamin (to include vitamins A, D, E, and K) at bedtime or 2 hours after orlistat dose
					- Eating >30% kcal from fat results in greater GI side effects
					- FDA-approved for children ≥12 years old
					- Administer levothyroxine and orlistat 4 hours apart

Lorcaserin (Belviq®) 2012	Serotonin (5HT2c) receptor agonist BLOSSOM BLOOM **1 yr: 3.0%-3.6%** **2 yr: 3.1%**	10 mg PO BID	• Headache • Nausea • Dizziness • Fatigue • Xerostomia • Dry eye • Constipation • Diarrhea • Back pain • Nasopharyngitis • Hyperprolactinemia	✓ Pregnancy and breastfeeding ✓ Serotonin syndrome or neuroleptic malignant syndrome • Safety data lacking in patients who have depression • Concomitant use of SSRI, SNRI, MAOI, bupropion, St. John's wort as may increase risk of developing serotonin syndrome • Uncontrolled mood disorder • Cognitive impairment • Avoid in patients with severe liver injury or renal insufficiency • Caution with patients with bradycardia, heart block, or heart failure • Unproven concern for potential cardiac valvulopathy • Leukopenia	**Monitor for:** • Symptoms of cardiac valve disease • Bradycardia • Serotonin syndrome • Neuroleptic malignant syndrome • Depression • Severe mood alteration, euphoria, dissociative state • Confusion/somnolence • Priapism • Leukopenia • Euphoria at high doses could predispose to abuse • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas
Phentermine/ Topiramate ER (Qsymia®) 2012	NE-releasing agent (phentermine) GABA receptor modulation (topiramate) EQUIP CONQUER SEQUEL **1 yr: 8.6%-9.3% on high dose; 6.6% on treatment dose** **2 yr: 8.7% on high dose; 7.5% on treatment dose**	**Starting dose:** 3.75/23 mg PO QD for 2 weeks **Recommended dose:** 7.5/46 mg PO QD **Escalation dose:** 11.25/69 mg PO QD **Maximum dose:** 15/92 mg PO QD	• Headache • Paresthesia • Insomnia • Decreased bicarbonate • Xerostomia • Constipation • Nasopharyngitis • Anxiety • Depression • Cognitive impairment (concentration and memory) • Dizziness • Nausea • Dysgeusia	✓ Pregnancy and breastfeeding (topiramate teratogenicity) ✓ Hyperthyroidism ✓ Acute angle-closure glaucoma ✓ Concomitant MAOI use (within 14 days) • Tachyarrhythmias • Decreased cognition • Seizure disorder • Anxiety and panic attacks • Nephrolithiasis • Hyperchloremic metabolic acidosis • Dose adjustment with hepatic and renal impairment • Concern for abuse potential • Combined use with alcohol or depressant drugs can worsen cognitive impairment	**Monitor for:** • Increased heart rate • Depressive symptomatology or worsening depression especially on maximum dose • Hypokalemia (especially with HCTZ or furosemide) • Acute myopia and/or ocular pain • Acute kidney stone formation • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas - Potential for lactic acidosis (hyperchloremic non-anion gap) in combination with metformin - MAOI (allow ≥14 days between discontinuation) - 15 mg/92 mg dose should not be discontinued abruptly (increased risk of seizure); taper over at least 1 week - Health care professional should check ßHCG before initiating, followed by monthly self-testing at home - Monitor electrolytes and creatinine before and during treatment - Can cause menstrual spotting in women taking birth control pills due to altered metabolism of estrogen and progestins

Anti-obesity Medication (Trade Name) Year of FDA Approval	Mechanism of Action, Study Name, Study Duration: % TBWL Greater Than Placebo	Dose	Common Side Effects	Contraindications, Cautions, and Safety Concerns	Monitoring and Comments
Naltrexone ER/ Bupropion ER (Contrave®) 2014	Opiate antagonist (naltrexone) Reuptake inhibitor of DA and NE (bupropion) COR-I COR-II COR-BMOD **1 yr: 4.2%-5.2%**	**Titrate dose:** **Week 1:** 1 tab (8/90 mg) PO QAM **Week 2:** 1 tab (8/90 mg) PO BID **Week 3:** 2 tabs (total 16/180 mg) PO QAM and 1 tab (8/90 mg) PO QHS **Week 4:** 2 tabs (total 16/180 mg) PO QHS	• Nausea • Headache • Insomnia • Vomiting • Constipation • Diarrhea • Dizziness • Anxiety • Xerostomia	✓ Pregnancy and breastfeeding ✓ Uncontrolled hypertension ✓ Seizure disorder ✓ Anorexia nervosa ✓ Bulimia nervosa ✓ Severe depression ✓ Drug or alcohol withdrawal ✓ Concomitant MAOI (within 14 days) ✓ Chronic opioid use • Cardiac arrhythmia • Dose adjustment for liver and kidney impairment • Narrow-angle glaucoma • Uncontrolled migraine disorder • Generalized anxiety disorder • Bipolar disorder • Safety data lacking in patients who have depression • Seizures (bupropion lowers seizure threshold)	**Monitor for:** • Increased heart rate and blood pressure • Worsening depression and suicidal ideation • Worsening of migraines • Liver injury (naltrexone) • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas • Seizures (bupropion lowers seizure threshold) - MAOI (allow ≥14 days between discontinuation) - Dose adjustment for patients with renal and hepatic impairment - Avoid taking medication with a high-fat meal - Can cause false positive urine test for amphetamine - Bupropion inhibits CYP2D6
Liraglutide 3 mg (Saxenda®) 2014	GLP-1 analog SCALE Obesity & Prediabetes **1 yr: 5.6%**	**Titrate dose weekly by 0.6 mg as tolerated by patient (side effects):** 0.6 mg SC QD→ 1.2 mg SC QD→ 1.8 mg SC QD→ 2.4 mg SC QD→ 3.0 mg SC QD	• Nausea • Vomiting • Diarrhea • Constipation • Headache • Dyspepsia • Increased heart rate	✓ Pregnancy and breastfeeding ✓ Personal or family history of medullary thyroid cancer or MEN2 ✓ Pancreatitis ✓ Acute gallbladder disease • Gastroparesis • Severe renal impairment can result from vomiting and dehydration • Use caution in patients with history of pancreatitis • Use caution in patients with cholelithiasis • Suicidal ideation and behavior • Injection site reactions	**Monitor for:** • Pancreatitis • Cholelithiasis and Cholecystitis • Hypoglycemia in patients having T2DM treated with insulin and/or sulfonylureas • Increased heart rate • Dehydration from nausea/vomiting • Injection site reactions - Titrate dose based on tolerability (nausea and GI side effects)

Abbreviations: BID = twice daily; DA = dopamine; FDA = US Food and Drug Administration; GI = gastrointestinal; HCTZ = hydrochlorothiazide; MAOI = monoxidase inhibitor; MEN2 = multiple endocrine neoplasia type 2; NE = norepinephrine; OTC = over-the-counter medication; % TBWL = percent total body weight loss from baseline over that observed in the placebo group; PO = oral; QAM = every morning; QD = daily; QHS = every bedtime; SC = subcutaneous; SNRI = serotonin–norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TID = 3 times a day; T2DM = type 2 diabetes mellitus.

FDA indication for all medications: BMI >30 kg/m^2 or BMI ≥27kg/m^2 with significant comorbidity.

After 3 to 4 months of treatment with antiobesity medication:

- **For naltrexone ER/bupropion ER and lorcaserin:**
  If the patient has not lost at least 5% of their baseline body weight at 12 weeks on the maintenance dose, the medication should be discontinued.
- **For phentermine/topiramate ER:**
  Continue medication if the patient has lost >5% body weight after 12 weeks on recommended dose (7.5 mg/42 mg); if the patient has not lost at least 3% of body weight after being on the recommended dose for 12 weeks then the medication should be discontinued, or the patient can be transitioned to maximum dose (15 mg/92 mg); if patient has not lost at least 5% after 12 additional weeks on the maximum dose, the medication should be discontinued.
- **For liraglutide 3 mg:**
  If the patient has not lost at least 4% of body weight 16 weeks after initiation, the medication should be discontinued.

References:
1–4 and package inserts for each medication

1. Wyatt HR. Update on treatment strategies for obesity. *J Clin Endocrinol Metab*. 2013;98(4):1299-1306.
2. Garvey WT, Garber AJ, Mechanick JI, Bray GA, Dagogo-Jack S, Einhorn D, et al. American Association of Clinical Endocrinologists and American College of Endocrinology position statement on the 2014 advanced framework for a new diagnosis of obesity as a chronic disease. *Endocr Pract*. 2014;20(9):977-989.
3. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA*. 2014;311(1):74-86.
4. Fujioka K. Current and emerging medications for overweight and obesity in people with comorbidities. *Diabetes Obes Metab*. 2015;17(11):1021-1032.