THE SOUTHERN DIABETES INITIATIVE

Beyond T2DM: How to Reduce Global Risk

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Faculty Disclosure Information

The following relationships exist related to this presentation:

Charles Vega, MD, FAAFP: No financial relationships to disclose.

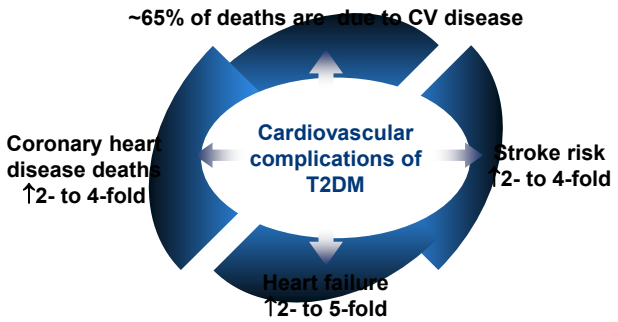
Off-Label/Investigational Discussion

In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Utilize guideline-recommended strategies to screen for and diagnose individuals with obesity, hypertension, and hyperlipidemia
- Identify effective lifestyle/behavioral modification that can benefit individuals with these comorbid conditions
- Apply guidelines and available efficacy/safety data to treat individuals with hypertension, hyperlipidemia, and obesity who are candidates for pharmacologic therapy

Cardiovascular Disease and Diabetes



Bell DSH. *Diabetes Care*. 2003;26:2433-41; Centers for Disease Control (CDC). www.cdc.gov.

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Hypertension

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Blood Pressure Screening and Treatment Goals

ADA

- Measure BP at every visit
- Goal <140/<90 mmHg
- Lower goal (<130/80 mmHg) recommended for patients with existing ASCVD or those with a 10-yr ASCVD risk >15%*

AACE/ACE

- Goal <130/<80 mmHg for most patients
- Individualize based on risk

ACC/AHA

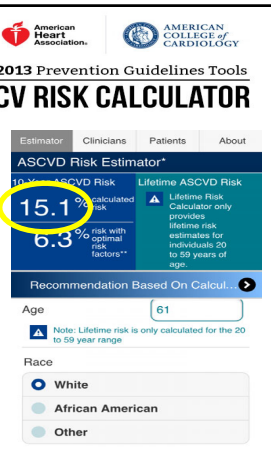
- Goal <130/80 mmHg in most individuals (including those with diabetes)
- (Goal not endorsed by ACP or AAFP)

*If goal can be achieved safely

ASCVD Risk Calculator

(ACC-AHA Pooled Cohort Equation)

- Gender
- Age
- Race
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Treatment for BP
- Diabetes
- Smoking



just google: ASCVD risk calculator

Stone NJ, et al. Circulation. 2013;129(25 Suppl 2):S1-S45.

Lifestyle Interventions

For all patients with **BP >120/80 mmHg**

- Weight loss if obese or overweight
- Increased physical activity
- DASH (Dietary Approaches to Stop Hypertension) diet
- Moderate alcohol intake (if drink alcohol)
- Reduce sodium

ADA. *Diabetes Care*. 2019: 42(1):S103-123.

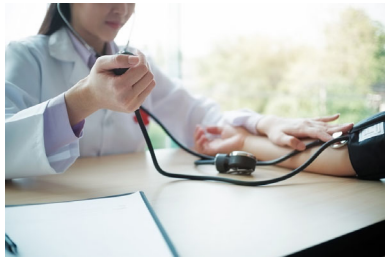
DASH Diet

Rich in fruits and vegetables (high potassium)
High in low fat dairy foods (high calcium)
Abundant in whole grains (high magnesium)

Pharmacologic Treatment of Hypertension in Patients with Diabetes

Selection of an antihypertensive regimen must take into account special circumstances, including:

CVD
Heart failure
Albuminuria
Race/ethnicity



Garber AJ, et al. Endocr Pract. 2018;24(1):91-120.

Pharmacologic Treatment of Hypertension in Patients with Diabetes

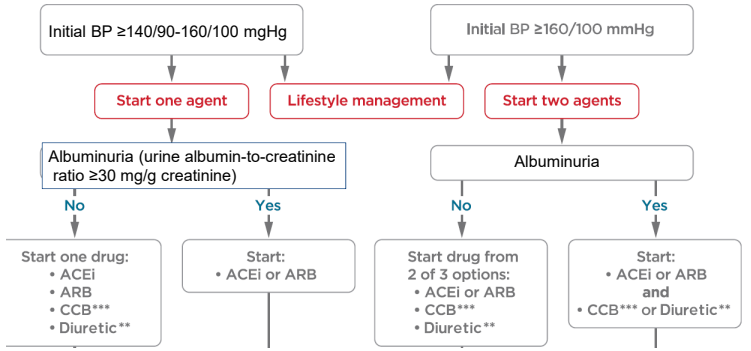
Use drug classes **demonstrated to reduce cardiovascular events in patients with diabetes**

- ACE inhibitors
- Angiotensin receptor blockers
- Long-acting thiazide-like diuretics (chlorthalidone and indapamide)
- Dihydropyridine calcium channel blockers

Level of evidence: A

ADA. *Diabetes Care*. 2019: 42(1):S103-123.

ADA Treatment Recommendations for Initial HTN Treatment in Patients with Diabetes



ADA. *Diabetes Care*. 2019: 42(1):S103-123. ---previous slide explains the asterisks

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ADA Recommendations for Treating Uncontrolled HTN in People with Diabetes

Reassess BP control (and adverse effects)

If not at goal titrate to max tolerated dose

Reassess

If still not at goal add another agent (ACEi or ARB, CCB, diuretic)

Reassess

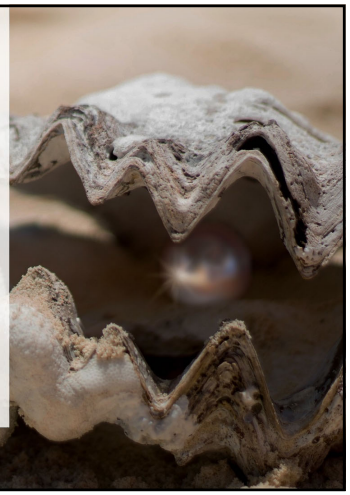
If not at goal with 3 med classes (including a diuretic) consider mineralocorticoid receptor agonist therapy

Do not use ACEi and ARBs together

ADA. *Diabetes Care*. 2019: 42(1):S103-123.

Clinical Pearls

- Intensive BP control provides greater benefit in patients with T2DM and others at higher baseline CV risk
- ADA BP goal for patients with T2DM
  - <130/80 mmHg if risk >15% or established ASCVD
  - <140/90 mmHg if risk <15%
- Lifestyle interventions represent important, but underutilized means to achieve BP control
- Pharmacologic therapy should utilize agents that reduce CV risk (and renal risk if albuminuria)
  - ACEi or ARB
  - CCB
  - Diuretic
- Titrate and add agents until BP goal is achieved



Hyperlipidemia

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When to Check a Lipid Profile in Patients with Diabetes

For patients not already on a statin

At time of diagnosis with T2DM

At an initial medial evaluation

Every 5 years (<40 years)

More frequently as appropriate (long duration of diabetes)

Immediately before starting a statin

4-12 weeks after starting a statin and after a dose change

ADA. *Diabetes Care*. 2019: 42(1):S103-123.

Is Fasting Necessary to Screen for Hyperlipidemia?

Adults ≥20 y/o not on drug Rx:

Measurement of either fasting or nonfasting lipid profile is useful for **estimating risk & documenting baseline LDL-C** (class I)

If initial nonfasting lipid profile reveals TG ≥ 400 → repeat lipid profile fasting for assessment of TG levels & baseline LDL-C (class I)

Grundy SM et al. 2018 ACC/AHA lipid guidelines. *J Am Coll Cardiol* 2019;73(24):3168-3209.

Lifestyle Interventions to Lower LDL-Cholesterol

Dietary Modification	Recommendation	LDL-C Reduction
Saturated fat	<7% calories	8%-10%
Dietary cholesterol	<200 mg/d	3%-5%
Plant stanols/sterols	Up to 2 g/d	6%-10%
Viscous dietary fiber	5-10 g/d	3%-5%
Soy protein	20-30 g/d	5%-7%
Almonds	>10 g/d	1%/10 g
Weight reduction	Lose 10 lb (4.5 kg)	5%-8%
Total		30%-45%

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *Circulation* 2002;106:3143-3421; Jenkins DJ et al. *JAMA* 2003;290:502-510; Ripsin CM et al. *JAMA*1992;267:3317-3325; Rambjor GS et al. *Lipids* 1996;31:S45-S49; Jones PJH. *Curr Atheroscler Rep* 1999;1:230-235; Lichtenstein AH. *Curr Atheroscler Rep* 1999;1:210-214.

ADA Recommendations for Dyslipidemia in Patients with Diabetes

All patients (**A**) → Lifestyle interventions

<40 years and additional CV risk factors (**C**)
40-75 years (**A**)
>75 years (**B**)
→ Moderate-intensity statin

Regardless of age

Multiple CV risk factors (**C**)
Established ASCVD or 10-year risk >20% (**A**)
→ High intensity statin

LDL ≥ 70 mg/dL on maximally-tolerated statin, consider adding (**A**) → Ezetimibe or PCSK9 inhibitor

ADA. *Diabetes Care*. 2018: 41(1):S103-123.

*Statins are contraindicated in pregnancy

Intensities of Statin Therapy

High Intensity	Moderate Intensity	Low Intensity
Lowers LDL-C on average by ≥50%	Lowers LDL-C on average by 30% to ≤50%	Lowers LDL-C on average by <30%
Atorvastatin 40*-80mg	Atorvastatin 10 (20) mg	Simvastatin 10 mg
Rosuvastatin 20 (40) mg	Rosuvastatin (5) 10 mg	Pravastatin 10-20 mg
	Simvastatin 20-40 mg†	Lovastatin 20 mg
	Pravastatin 40 (80) mg	Fluvastatin 20-40 mg
	Lovastatin 40 mg	Pitavastatin 1 mg
	Fluvastatin XL 80 mg	
	Fluvastatin 40 mg bid	
	Pitavastatin 2-4 mg	

Stone NJ et al. *J Am Coll Cardiol* 2014;63:2889-2934

Ezetimibe

IMPROVE-IT Trial

Adding ezetimibe to a statin improved outcomes patients with DM

- 24% relative reduction MI
- 39% relative reduction in ischemic stroke

Cannon CP et al. *NEJM* 2015;372:2387-2397; Giugliano R, et al. Circulation. 2017;137:1571-1582.

PCSK9 Inhibitors –CV Outcomes Trials

Evolocumab - FOURIER trial

- 15% RRR in primary outcome
- 20% RRR in stroke/CV death

Alirocumab – ODYSSEY trial

- 15% RRR in primary outcome
- 15% RRR in all cause mortality

PCSK9 = Proprotein convertase subtilisin/kexin type 9 RRR = relative risk reduction

Sabatine MS et al. N Engl J Med. 2017;376:1713-1722; ACC Scientific Sessions 2018; Szarek M, et al. J Am Coll Cardiol. 2019;73(4):387-396.

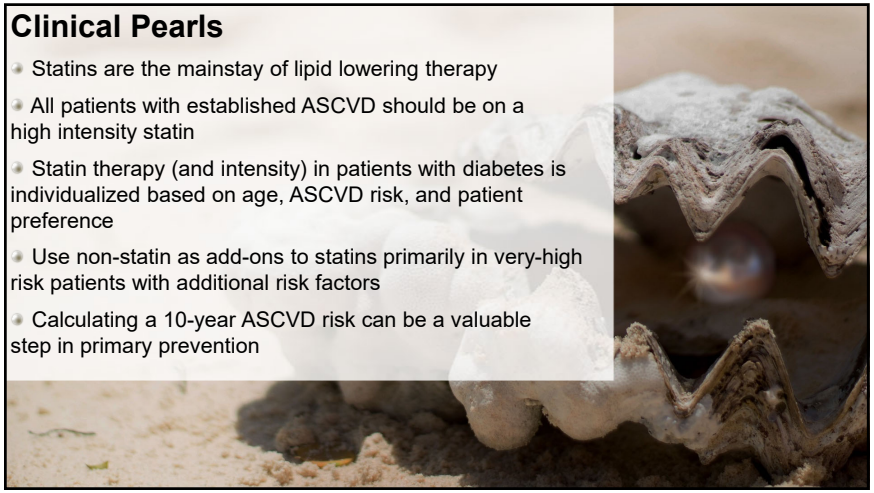
Don't Forget Triglycerides

TGs ≥150 mg/dL	Optimize **glycemic control** and lifestyle
Fasting TGs ≥500 mg/dL	Look for **secondary causes** Consider therapy to decrease risk of pancreatitis (**fibrate**)
Fasting TGs 175-499 mg/dL	Treat and address: **Lifestyle factors** (obesity, metabolic syndrome) Secondary factors (diabetes, CKD, chronic liver disease, hypothyroidism, nephrotic syndrome) **Medications that increase TGs**

ADA. *Diabetes Care*. 2018: 42(1):S103-123.

Clinical Pearls

- Statins are the mainstay of lipid lowering therapy
- All patients with established ASCVD should be on a high intensity statin
- Statin therapy (and intensity) in patients with diabetes is individualized based on age, ASCVD risk, and patient preference
- Use non-statin as add-ons to statins primarily in very-high risk patients with additional risk factors
- Calculating a 10-year ASCVD risk can be a valuable step in primary prevention



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Obesity

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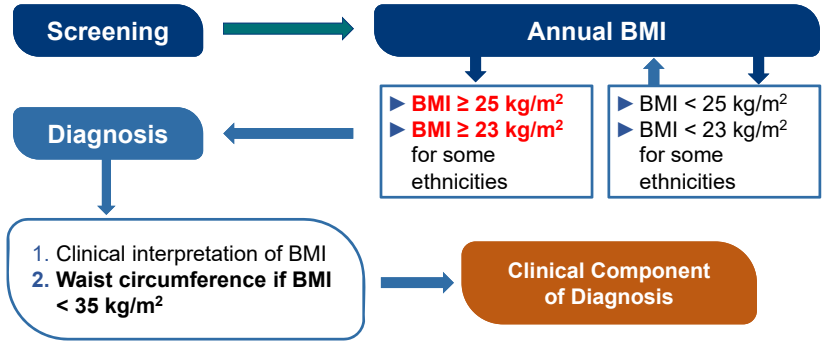
Diagnosis & Assessment of Obesity



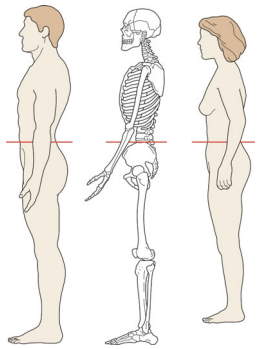
Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.

Waist Circumference

Only necessary for BMI < 35 kg/m²

Abnormal: ♀ ≥ 40in ♂ ≥ 35in*

1) Locate upper hip bone and top of right iliac crest
2) Place measuring tape around abdomen at level of iliac crest, keeping it parallel to the floor
3) Ensure tape is snug but not compressing the skin



*Values for Caucasians. Cutoffs are lower for some ethnic groups such as South Asians and East Asians

http://www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf. Accessed April 18, 2018.

Classification of Obesity by BMI and Waist Circumference

Classification	BMI		Waist	
			Waist Circumference and Comorbidity Risk	
	BMI (kg/m²)	Comorbidity Risk	Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >35 in (88 cm)
Underweight	<18.5	Low but other problems		
Normal Weight	18.5-24.9	Average		
Overweight	25-29.9	Increased	Increased	High
Overweight class I	**30-34.9**	**Moderate**	**High**	**Very high**
Overweight class II	35-39.9	Severe	Very high	Very high
Overweight class III	≥40	Very severe	Extremely high	Extremely high

World Health Organization.

Weight Loss Goal

2019 ADA: For patients with type 2 diabetes who are overweight or obese and ready to achieve weight loss: diet, physical activity, and behavioral therapy designed to achieve and maintain **>5%** weight loss should be prescribed. **A**

ADA. *Diabetes Care*. 2019;42(1):S81-89.

Medical Diagnosis of Obesity

Anthropometric Component	Candidates for Weight Loss Therapy	Patients Present with Weight-related Disease of Complication (Clinical Component)	
Patients present with **BMI ≥ 25 kg/m²** or **BMI ≥ 23 kg/m²** in certain ethnicities, and excess adiposity	Evaluate for weight-related complications →	Prediabetes	PCOS
		Metabolic syndrome	Female infertility
		T2DM	Male hypogonadism
		Dyslipidemia	Obstructive sleep apnea
		Hypertension	Asthma/reactive airway disease
	← Evaluate for overweight or obesity	CVD	Osteoarthritis
		NFLD	Urinary stress incontinence
		GERD	Depression

Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.

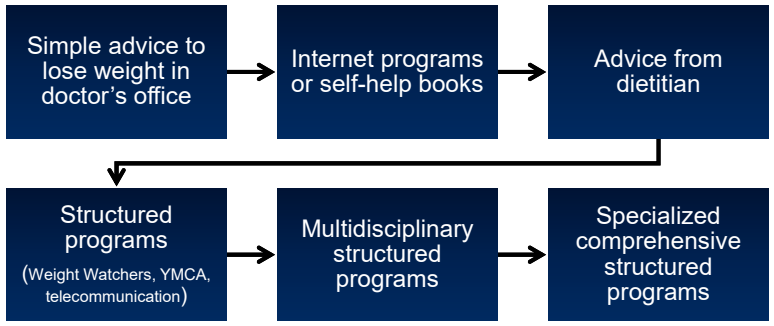
Treatment Goals

Initial weight loss goal (for most patients)
5% loss in first 3 months

Increase in muscle mass may be more important than decrease in fat mass

Long-term goal (if desired): additional energy deficit recalculated for the next weight loss goal

Intensification of Lifestyle Therapy



Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.

Weight Loss Diets

Diet/Program	Description
Weight Watchers	Point system based encourages healthy choices
Jenny Craig	Prepackaged meals, lifestyle/behavior support, consultants
Volumetrics	Focus on low-density, high-volume foods
Health Management Resources	Meal replacements, fruits/vegetables; physical exercise
Biggest Loser	Regular meals (fruits, vegetables, lean protein, whole grains), portion control, food journal, exercise
Flexitarian	Mostly vegetarian
Raw food	Raw foods (fresh fruits, berries, vegetables, nuts, seeds, herbs)
Slim-Fast	Meal replacement program
Vegan diet	Excludes all animal products

When to Initiate Weight Loss Medications

Initiate Lifestyle Therapy if…

NO COMPLICATIONS
Overweight or obesity with no clinically significant weight-related complications (secondary prevention)

MILD TO MODERATE COMPLICATIONS
Mild-moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to ameliorate the complication (tertiary prevention)

Initiate Weight Loss Medication as an Adjunct to Lifestyle Therapy if…

FAILURE ON LIFESTYLE THERAPY
Progressive weight gain or failure to achieve clinical improvement in weight-related complications on lifestyle therapy alone

WEIGHT REGAIN ON LIFESTYLE THERAPY
Overweight (BMI 27-29 kg/m^2) or obesity with weight regain following initial success on lifestyle therapy alone

PRESENCE OF WEIGHT-RELATED COMPLICATIONS
Overweight (BMI 27-29 kg/m^2) or obesity with weight-related complications, particularly if severe

Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.

Weight Loss Medications

2019 ADA:
Weight-loss medications are effective as adjuncts to diet, physical activity, and behavioral counseling for selected patients with type 2 diabetes and BMI ≥27 kg/m^2. **A**

Potential benefits must be weighed against the potential risks of the medications. **A**

ADA. *Diabetes Care*. 2019;42(1):S81-89.

Agents for Short-term Weight Management: *Dosing*

Benzphetamine	**Initial**: 25 mg once daily; may titrate up to 25 to 50 mg one to three times daily. **Maximum dose**: 50 mg three times daily.
Diethylpropion	**Immediate release**: 25 mg three times daily before meals. **Controlled release**: 75 mg every morning.
Phentermine	**Immediate release**: 15 to 37.5 mg daily or divided twice-daily. **Orally disintegrating tablet (ODT)**: 15 to 37.5 mg once daily in AM
Phendimetrazine	**Immediate release**: 17.5 to 35 mg two or three times daily, one hour before meals. **Maximum dose**: 70 mg three times daily. **Sustained release**: 105 mg daily in the morning.

Agents for Short-term Weight Management: *Adverse Effects and Precautions*

Applies to all sympathomimetic agents

ADVERSE EFFECTS: Increase in HR, BP, insomnia, dry mouth, constipation, nervousness

AVOID: Heart disease, poorly controlled HTN, pulmonary HTN, or h/o addiction or drug abuse.

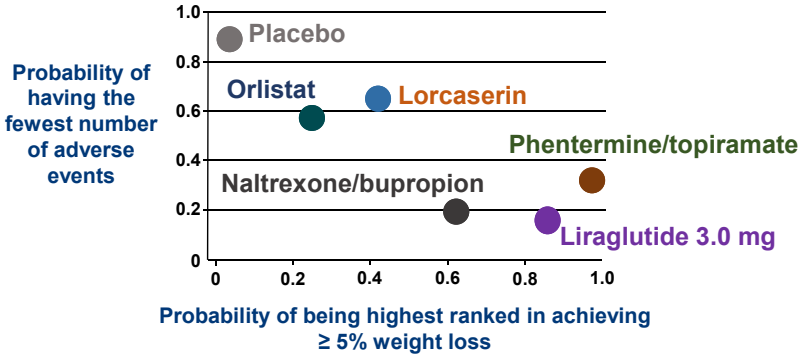
CONTRAINDICATIONS: h/o CVD, hyperthyroidism, glaucoma, MAOI therapy, agitated states, pregnancy, or breastfeeding

✷✷✷ **Limit to short-term use (≤ 12 weeks)** ✷✷✷

Agents for Long-term Weight Management

Medication	Mechanism of Action	Year Approved
Orlistat (Xenical™; Alli™- OTC)	Lipase inhibitor	1999
Lorcaserin (Belviq®)	Serotonin (5HT2c) receptor agonist	2012
Phentermine/ Topiramate ER (Qsymia®)	NE-releasing agent (phentermine) GABA receptor modulation (topiramate)	2012
Naltrexone ER/ Bupropion ER (Contrave®)	Opiate antagonism (naltrexone) Reuptake inhibitor of DA and NE (bupropion)	2014
Liraglutide 3.0 mg (Saxenda®)	GLP-1 receptor agonist	2014

Efficacy vs. Adverse Events of Agents for Long-term Weight Management



Khera R, et al. *JAMA*. 2016;315:2424-2434.

Agents for Long-term Weight Management: *Dosing*

Indications (*All Medications*)
- Weight loss and weight maintenance in conjunction with a reduced calorie diet
- BMI ≥ 30 kg/m^2
- BMI ≥ 27 kg/m^2 with ≥ 1 weight-related comorbidity
  - Hypertension
  - T2DM
  - Dyslipidemia

Orlistat[1]	**Prescription**:120 mg TID with each main meal containing fat, taken during the meal or up to 1 hour after eating **OTC:** 60 mg TID with each meal
Lorcaserin[2]	► 10 mg twice daily or 20mg XR daily ► Discontinue if 5% weight loss is not achieved within 12 weeks

Xenical prescribing information. South San Francisco, CA: Genentech USA, Inc.; 2013. (2) Belviq prescribing information. Woodcliff Lake, NJ: Eisai Inc.; 2012.

Phentermine/ Topiramate ER[1]	▶ Once daily in morning ▪ **Starting dose**: phentermine 3.75/topiramate ER 23 mg for 14 days ▪ **Usual dose**: 7.5/46 mg ▪ **Maximum dose**: 15/92 mg ▶ If < 3% weight loss after 12 weeks on usual dose → either discontinue medication or advance to maximum dose (transition dose phentermine 11.25 mg/topiramate ER 69 mg
Naltrexone/ Bupropion SR[2]	▶ Titrated to 2 tablets twice a day ▶ Each tablet contains naltrexone 8 mg/bupropion 90 mg
Liraglutide 3 mg[3]	▶ Initiate at 0.6 mg SC QD for 1 week ▶ Increase by 0.6 mg/day in weekly intervals until a dose of 3 mg/day is achieved

Qsymia prescribing information. Mountain View, CA: Vivus, Inc.; 2012. Contrave prescribing information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; 2014. (3) Saxenda prescribing information. Plainsboro, NJ: NovoNordisk Inc.

Agents for Long-term Weight Management: *Adverse Effects*

Most Common Adverse Effects

ORLISTAT[1]: diarrhea, flatulence, leakage of oily stools, abdominal pain

LORCASERIN[2]: constipation, nausea, cough, dizziness, dry mouth, fatigue, headaches

PHENTERMINE/TOPIRAMATE ER[3]: constipation, dizziness, dry mouth, taste changes (especially with carbonated beverages), tingling in hands and feet, trouble sleeping

) Xenical prescribing information. South San Francisco, CA: Genentech USA, Inc.; 2013. (2) Belviq prescribing information. Woodcliff Lake, NJ: Eisai Inc.; 2012. (3) Qsymia prescribing information. Mountain View, CA: Vivus, Inc.; 2012.

Agents for Long-term Weight Management: *Adverse Effects*

Most Common Adverse Effects

NALTREXONE-BUPROPION[1]: constipation, nausea, vomiting, diarrhea, dizziness, dry mouth, headache, ↑ BP, ↑ HR, insomnia, hepatic damage

LIRAGLUTIDE[2]: nausea, diarrhea, constipation, abdominal pain, dizziness, headache

(1) Contrave prescribing information. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; 2014. (2) Saxenda prescribing information. Plainsboro, NJ: NovoNordisk Inc.

Individualization of Therapy

Consideration	Orlistat	Lorcaserin	Phentermine/ Topiramate	Naltrexone ER/ Bupropion ER	Liraglutide 3 mg
Prevent T2DM		Insufficient data		Insufficient data	
T2DM					
Severe renal impairment (eGFR < 30 mL/min)	Oxalate nephropathy	Urinary clearance of drug or metabolite			Avoid vomiting & volume depletion
Nephrolithiasis	Calcium oxalate stones		Calcium phosphate stones		
Depression		Insufficient data Avoid serotonergic drugs	Avoid max dose (15 mg/92 mg QD)	Insufficient data Avoid in adolescents/ young adults	

Preferred Use with caution Avoid

Garvey WT, et al. Endocr Pract. 2016 Jul;22 Suppl 3:1-203.

Consideration	Orlistat	Lorcaserin	Phentermine/ Topiramate	Naltrexone ER/ Bupropion ER	Liraglutide 3 mg
Psychoses	Insufficient data	Insufficient data			Insufficient data
Glaucoma			Contraindicated; may trigger angle closure	May trigger angle closure	
Seizure			15/92 mg—taper slowly to stop	Bupropion lowers seizure threshold	
Pancreatitis	Monitor				Monitor Cases with history
Opioid use				Will antagonize opioids/opiates	
Age ≥ 65 years	Limited data	Insufficient data	Limited data	Insufficient data	Limited data
Alcoholism/addiction		Abuse potential (high dose)?	Insufficient data; (TOP benefit?)	Seizure risk	

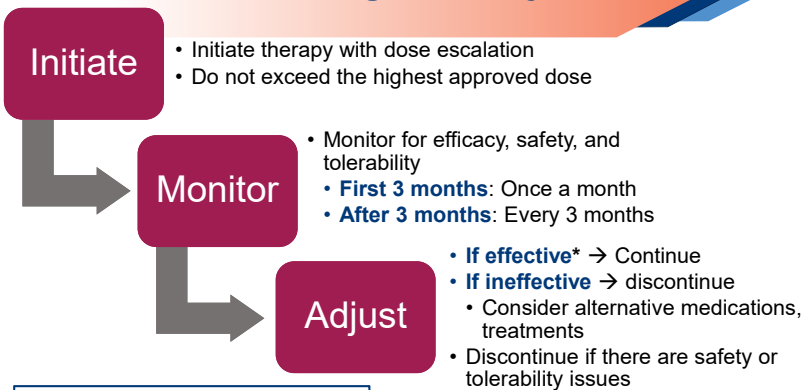
Individualization of Therapy for CVD

Consideration	Orlistat	Lorcaserin	Phentermine / Topiramate	Naltrexone ER/ Bupropion ER	Liraglutide 3 mg
CAD			✓ HR	✓ HR, BP	✓ HR
Arrhythmia		✓ for bradycardia	✓ HR, rhythm	✓ HR, rhythm, BP	✓ HR, rhythm
CHF	Insufficient data				
Hypertension			✓ HR	✓ HR, BP Contraindication Uncontrolled HTN	✓ HR

Preferred Use with caution Avoid

Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.

Treatment Monitoring and Adjustment



*Effective = Weight loss ≥ 5% at 3 months

Apovian CM, et al. *J Clin Endocrinol Metab*. 2015;100:342-362; ADA. *Diabetes Care*. 2019;42(1):S81-89.

When to Consider Metabolic Surgery?

2019 ADA: For adults with T2DM who are appropriate surgical candidates, metabolic surgery

Should be recommended as a treatment option in patients with:

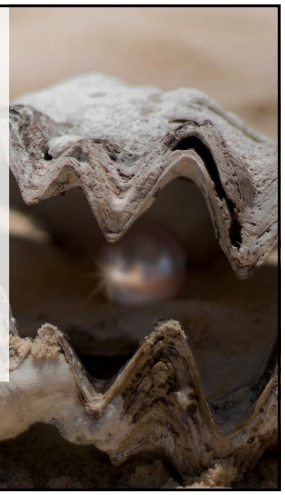
- BMI ≥40 kg/m^2 (BMI ≥37.5 kg/m^2 in Asian Americans). **A**
- BMI 35.0–39.9 kg/m^2 (32.5–37.4 kg/m^2 in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with reasonable nonsurgical methods. **A**

May be considered in patients with:

- BMI 30.0–34.9 kg/m^2 (27.5–32.4 kg/m^2 in Asian Americans) who do not achieve durable weight loss and improvement in comorbidities with reasonable nonsurgical methods. **A**

ADA. *Diabetes Care*. 2019;42(1):S81-89.

Clinical Pearls



All adult patients should be screened for overweight and obesity

- **BMI**
- **WC:** If BMI < 35 kg/m^2
  - **Abnormal WC:** ♀ ≥ 40in ♂ ≥ 35in

Initiation of drug therapy should be individualized

Choice of medication depends on complications, side effect profile of medications, warnings and cautions, and other aspects of medical history in an individual patient

Candidates for drug therapy

- BMI ≥ 30 kg/m^2
- BMI of 27-29.9 kg/m^2 with complications

The End

A---.

Lifestyle Interventions to Lower LDL-Cholesterol

Dietary Modification	Recommendation	LDL-C Reduction
Saturated fat	<7% calories	8%-10%
Dietary cholesterol	<200 mg/d	3%-5%
Plant stanols/sterols	Up to 2 g/d	6%-10%
Viscous dietary fiber	5-10 g/d	3%-5%
Soy protein	20-30 g/d	5%-7%
Almonds	>10 g/d	1%/10 g
Weight reduction	Lose 10 lb (4.5 kg)	5%-8%
Total		30%-45%

Ripsin CM et al. *JAMA* 1992;267:3317-3325,
Rambjor GS et al. *Lipids* 1996;31:S45-S49
Jones PJH. *Curr Atheroscler Rep* 1999;1:230-235
Lichtenstein AH. *Curr Atheroscler Rep* 1999;1:210-214

Expert Panel on Detection, Evaluation, and Treatment of Hig
Blood Cholesterol in Adults. *Circulation* 2002;106:3143-3421
Jenkins DJ et al. *JAMA* 2003;290:502-510

Drugs That Cause Weight Gain

Category	Drugs That May Cause Weight Gain	Possible Alternatives
Neuroleptics	Thioridazine, haloperidol, olanzapine, quetiapine, risperidone, clozapine	Ziprasidone, aripiprazole
Antidiabetic agents	Insulin, sulfonylureas, thiazolidinediones	AGIs, DPP-4is, SGLT2is, GLP-1 RAs, metformin
Steroid hormones	Contraceptives, glucocorticoids, progestational steroids	Barrier methods, NSAIDs
Tricyclic antidepressants	Amitriptyline, nortriptyline, imipramine, doxepin	Protriptyline, bupropion, nefazodone
MAOIs	Phenelzine	
SSRIs	Paroxetine	Fluoxetine, sertraline
Other antidepressants	Mirtazapine, duloxetine	Bupropion
Anticonvulsants	Valproate, carbamazepine, gabapentin, pregabalin, vigabatrin	Topiramate, lamotrigine, zonisamide, felbamate
Antihistamines	Cyproheptadine	Inhalers, decongestants
β- and α-blockers	Propranolol, doxazosin	ACEi, CCBs

Kushner RF, Ryan DH. *JAMA*. 2014;312:943-952; Apovian CM, et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

Lifestyle Therapy

MEAL PLAN	PHYSICAL ACTIVITY	BEHAVIOR
• 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	• 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	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

Garvey WT, et al. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.