WHAT YOU NEED TO KNOW ABOUT MANAGING CARDIOVASCULAR RISK FACTORS

Nancy Chia, PharmD, MBA, BCPS
Clinical Pharmacist
Diamond Pharmacy Services – Drug Information Center
OPTICS Clinical Team

Disclosure

"I do not have any relevant financial relationships with any commercial interests."

- This informational presentation was developed by independent experts. The information provided in this presentation is not the official position or recommendation of NCCHC but rather expert opinion. This information is not intended to be appropriate for every clinical situation nor does it replace clinical judgment.
- NCCHC does not endorse or recommend any products or services mentioned

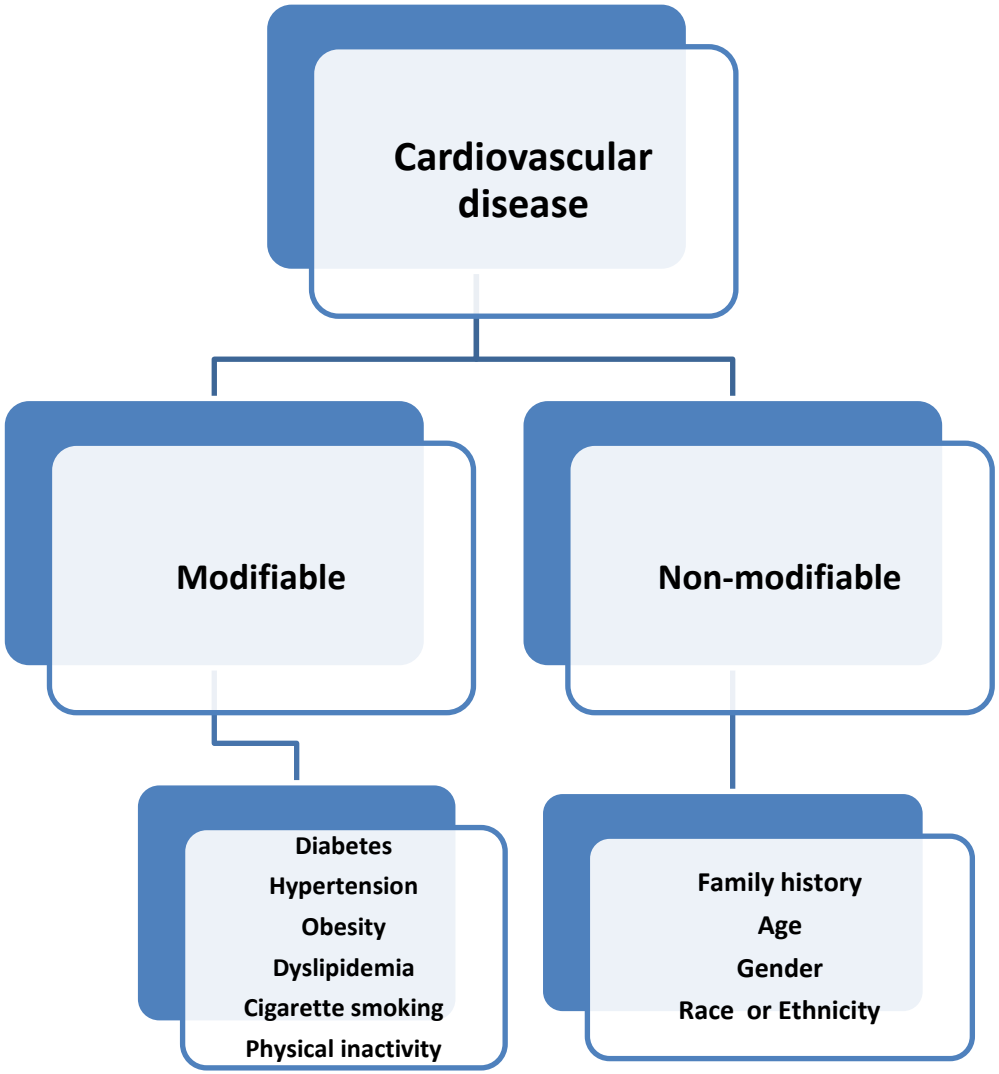
Objectives

- Review processes for assessing cardiovascular risk factors
- List preventive measures that reduce the risk of cardiovascular events
- Summarize treatment options for patients with cardiovascular risk factors

Introduction

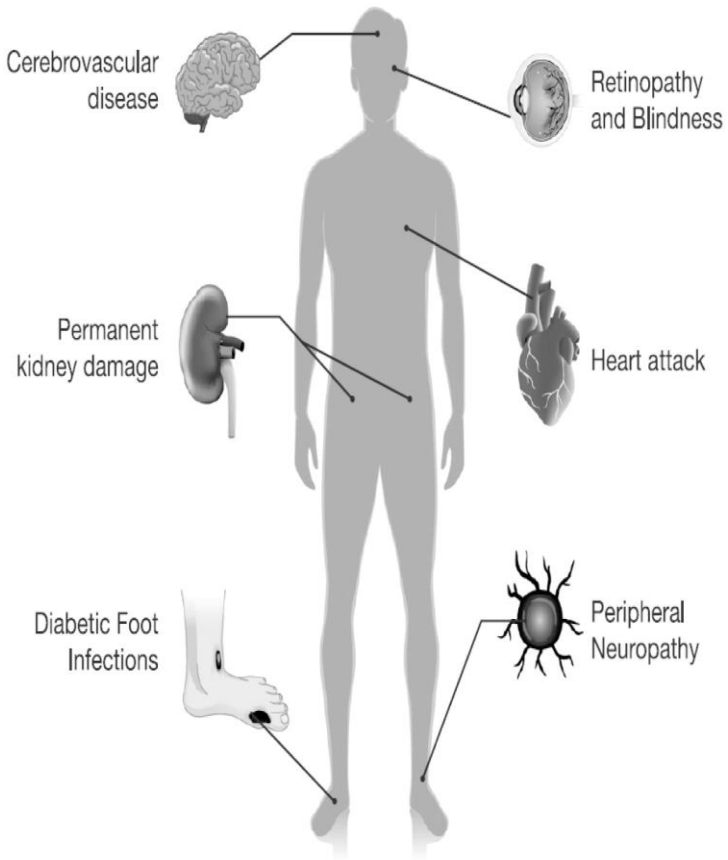
- Cardiovascular disease (CVD) is common in the general population worldwide, affecting the majority of adults 60 years and older.
- 17.9 million people die each year from CVDs.
  - An estimated 32% of all deaths worldwide.
- The American Heart Association (AHA) reported that 48% of adults (≥20 years) in the United States have CVD.
- By 2035, more than 130 million adults or 45.1% of the US population, are projected to have some form of CVD.
- Total costs of CVD are expected to reach 1.1 trillion in 2035.

Cardiovascular Risk Factors



Diabetes

- Cardiovascular disease (CVD), is the **number one cause of death** in people living with diabetes.
  - 2/3 of deaths in people with type 2 diabetes.
- People with diabetes are twice as likely to have heart disease or a stroke than people without diabetes.



Screening for diabetes and prediabetes

1. Testing should be considered in adults with overweight or obesity (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 35 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
6. People with HIV

CVD, cardiovascular disease; GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Classification and Diagnosis of Diabetes: s*tandards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S17-S38

Classification and Diagnosis of Diabetes

Type 2 diabetes	Prediabetes
Hemoglobin A1C ≥ 6.5% ***OR*** Fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L) ***OR*** Two-hour plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during 75 g oral glucose tolerance test ***OR*** In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).	Hemoglobin A1C of 5.7% to 6.4% ***OR*** Fasting plasma glucose of 100 to 125 mg/dL ***OR*** Two-hour plasma glucose 140 mg/dL (7.8 mmol/L) to 199mg/dL (11.0 mmol/L) during 75 g oral glucose tolerance test

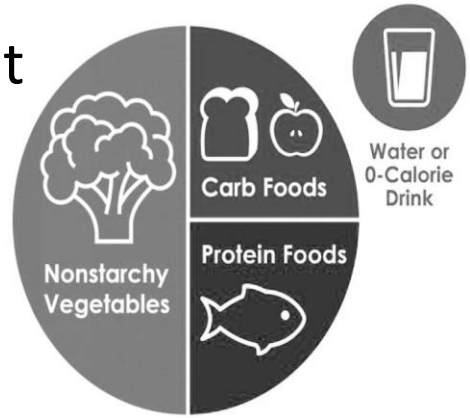
Classification and Diagnosis of Diabetes: S*tandards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S17-S38

ADA Standard Diabetes Medical Care

- **A1C <7** (every 3-6 months)
  - Recent diagnosis with long life expectancy and no CVD → **6-6.5 A1C**
  - Fasting and pre-meals **80-130** (hypoglycemia≤70)
  - 2 hours post meals **<180**
- Nephrology (annually)
- Dental (biannually)
- Comprehensive (diabetic) eye exam (Every 1-2 years)
- Comprehensive foot exam (annually; every visit if at risk)
- Vaccines:
  - Influenza vaccine- annually
  - Pneumonia
  - Hep B
  - HPV
  - TDAP
  - Zoster (>50 years old)

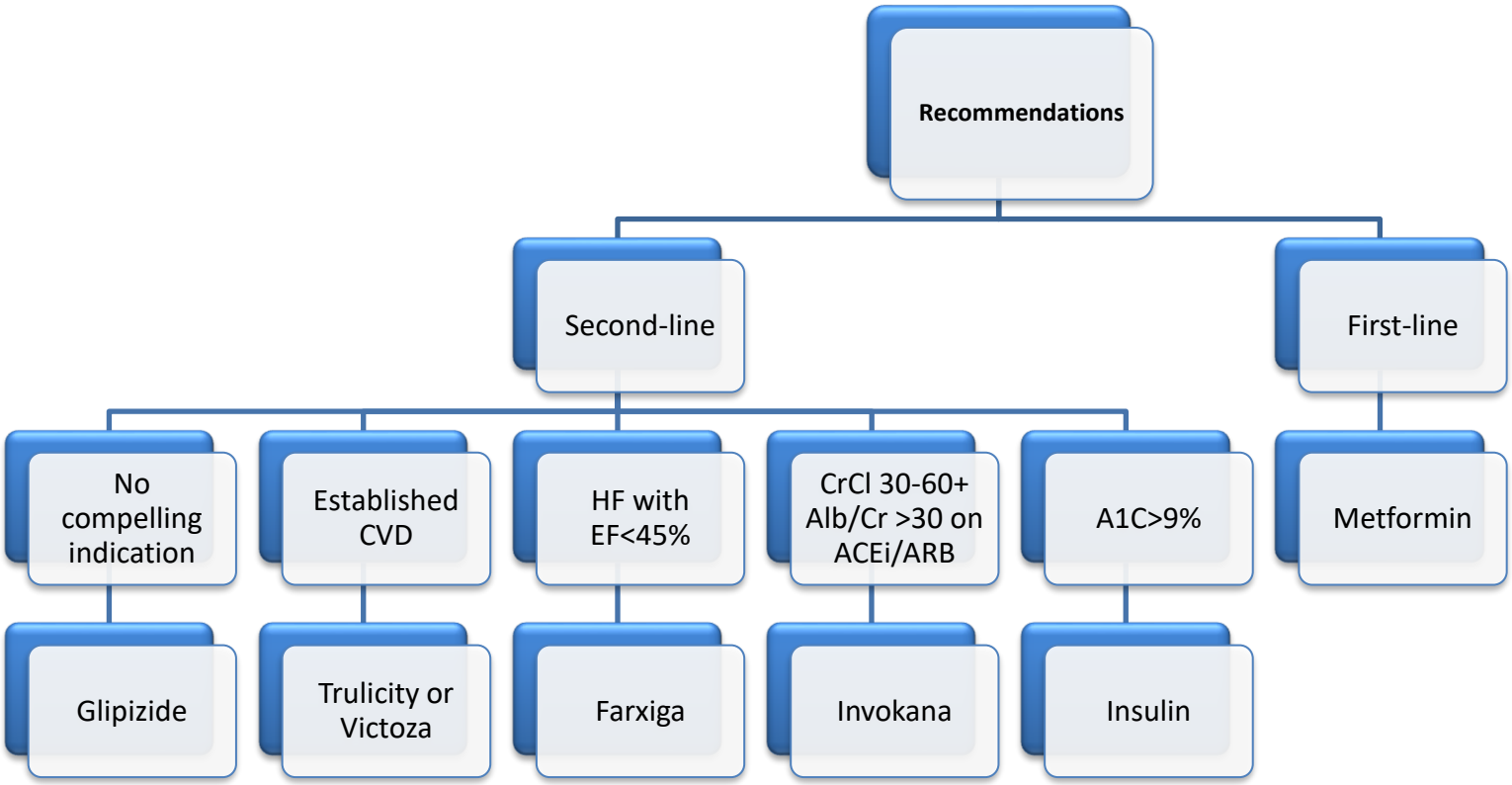
Treatment Recommendations-Non drug Therapy

- Emphasis lifestyle changes through diet, behavioral therapy, and exercise
  - 150 min/week of moderate-intensity aerobic exercise is recommended
  - Achieve and maintain 5% weight loss
  - Nutrient-dense healthful food choices such as whole grains, vegetables, fruits, legumes, low-fat dairy, lean meats, and nuts and seeds
- Diabetes self-management education and support is an essential component of successful diabetes management



	Efficacy	Hypoglycemia	Weight change	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
				ASCVD	HF			Progression of DKD	Dosing/use considerations*	
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30 mL/min/1.73 m^2	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin†	Benefit: empagliflozin‡, canagliflozin, dapagliflozin‡, ertugliflozin	High	Oral	Benefit: canagliflozin§, empagliflozin, dapagliflozin§	▪ See labels for renal dose considerations of individual agents ▪ Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	▪ Should be discontinued before any scheduled surgery to avoid potential risk for DKA ▪ DKA risk (all agents, rare in T2D) ▪ Risk of bone fractures (canagliflozin) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs	High	No	Loss	Benefit: dulaglutide†, liraglutide†, semaglutide (SQ)† Neutral: exenatide once weekly, lixisenatide	Neutral	High	SQ; oral (semaglutide)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: liraglutide, semaglutide (SQ), dulaglutide	▪ See labels for renal dose considerations of individual agents ▪ No dose adjustment for dulaglutide, liraglutide, semaglutide ▪ Caution when initiating or increasing dose due to potential risk of nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting severe adverse GI reactions when initiating or increasing dose of therapy.	▪ **FDA Black Box:** Risk of thyroid C-cell tumors in rodents; human relevance not determined **(liraglutide, dulaglutide, exenatide extended release, semaglutide)** ▪ GI side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected. ▪ Joint pain
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	▪ No dose adjustment required ▪ Generally not recommended in renal impairment due to potential for fluid retention	▪ **FDA Black Box:** Congestive heart failure **(pioglitazone, rosiglitazone)** ▪ Fluid retention (edema; heart failure) ▪ Benefit in NASH ▪ Risk of bone fractures ▪ Bladder cancer (pioglitazone) ▪ ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	▪ Glyburide: generally not recommended in chronic kidney disease ▪ Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	▪ FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin — Human insulin	High	Yes	Gain	Neutral	Neutral	Low (SQ)	SQ; inhaled	Neutral	▪ Lower insulin doses required with a decrease in eGFR; titrate per clinical response	▪ Injection site reactions ▪ Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulin — Analogs						High	SQ			

Treatment Recommendations



Patient Case #1

- In a discussion about weight loss with a patient who has type 2 diabetes and is overweight, what percentage of current weight should be the initial target for weight reduction during the course of 6 months?
  - 0.5%
  - 1%
  - 5%
  - 20%
  - 30%

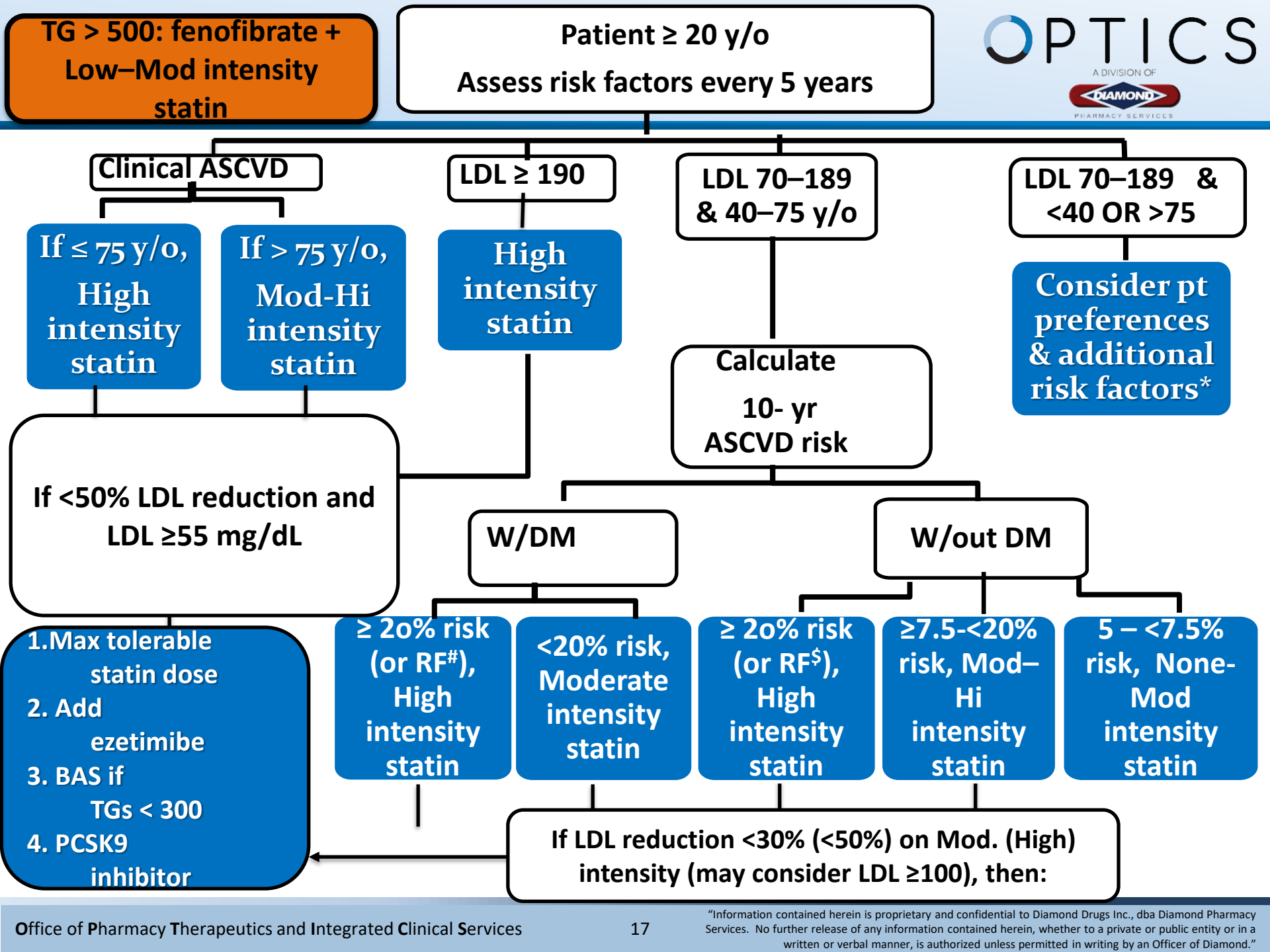
Dyslipidemia

- Atherosclerosis
  - Organ damage
  - Transient ischemic attack (TIA)
  - Stroke
  - Myocardial infarction (MI)
  - Chronic heart disease (CHD)

Diabetes Impact

- Causes dyslipidemia:
  - ↑Triglycerides↓ HDL ↑LDL
- Control glucose to bring TG levels under control
- For every 1% ↓ HgA1c (absolute drop) for patients with HgbA1c >8%, there is ~ 10% reduction for TG >150 mg/dL

Grundy SM. Et all. Definition of metabolic syndrome: report of the National, Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation. 2004;109:433-438



Intensity Classification of Statin Therapy

Intensity Level	Fluvastatin	Lovastatin	Pravastatin	Simvastatin	Atorvastatin	Rosuvastatin
Low (<30%)	20 mg		10 mg			
	40 mg	20 mg	20 mg	10 mg		
Moderate (30 - 49%)	80 mg	40 mg	40 mg	20 mg	10 mg	5 mg
		80 mg	80 mg	40 mg	20 mg	10 mg
High (≥50%)					40 mg	20 mg
					80 mg	40 mg

Antiplatelet Agents

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease.
- For patients with atherosclerotic cardiovascular disease and documented aspirin allergy, clopidogrel (75 mg/day) should be used.
- Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with diabetes who are at increased cardiovascular risk, after a comprehensive discussion with the patient on the benefits versus the comparable increased risk of bleeding.

Patient Case #2

- A 45-year-old patient has a past medical history of diabetes, hypertension, depression, and tobacco abuse. He had a history of TIA 3 years ago, and his LDL cholesterol is 140 mg/dL. The decision is made to initiate statin therapy. Which of the following doses of statin would be most appropriate?
  - Atorvastatin 10 mg
  - Rosuvastatin 40 mg
  - Simvastatin 40 mg
  - Pravastatin 80 mg

Hypertension

- In patients w/ HTN & additional CVD risk factors, 12 mmHg SBP ↓ over 10 years will prevent 1 death for every 11 patients treated

CVD	Average % Reduction
Stroke Incidence	35 – 40%
Myocardial infarction	20 – 25%
Heart Failure	50%

Target Organ Damage

- **Heart**
  - LVH, angina, MI, HF
- **Brain**
  - Stroke, TIA
- **Kidney**
  - CKD
- **Vasculature**
  - PAD
- **Eyes**
  - Retinopathy

Staging

BP Category	SBP		DBP
Normal	<120	And	<80
Elevated	120-129	And	<80
Hypertension			
Stage 1	130-139	Or	80-89
Stage 2	≥140	Or	≥90

Blood Pressure Goals

Population	ASCVD Risk	BP Goal
General	≥ 10%	<130/80
	< 10% (Or < 40y/o)	<140/90 (<130/80 "may be reasonable")
CVD or CKD	n/a	<130/80

Initial BP >130/80 mmHg and <150/90 mmHg

↓

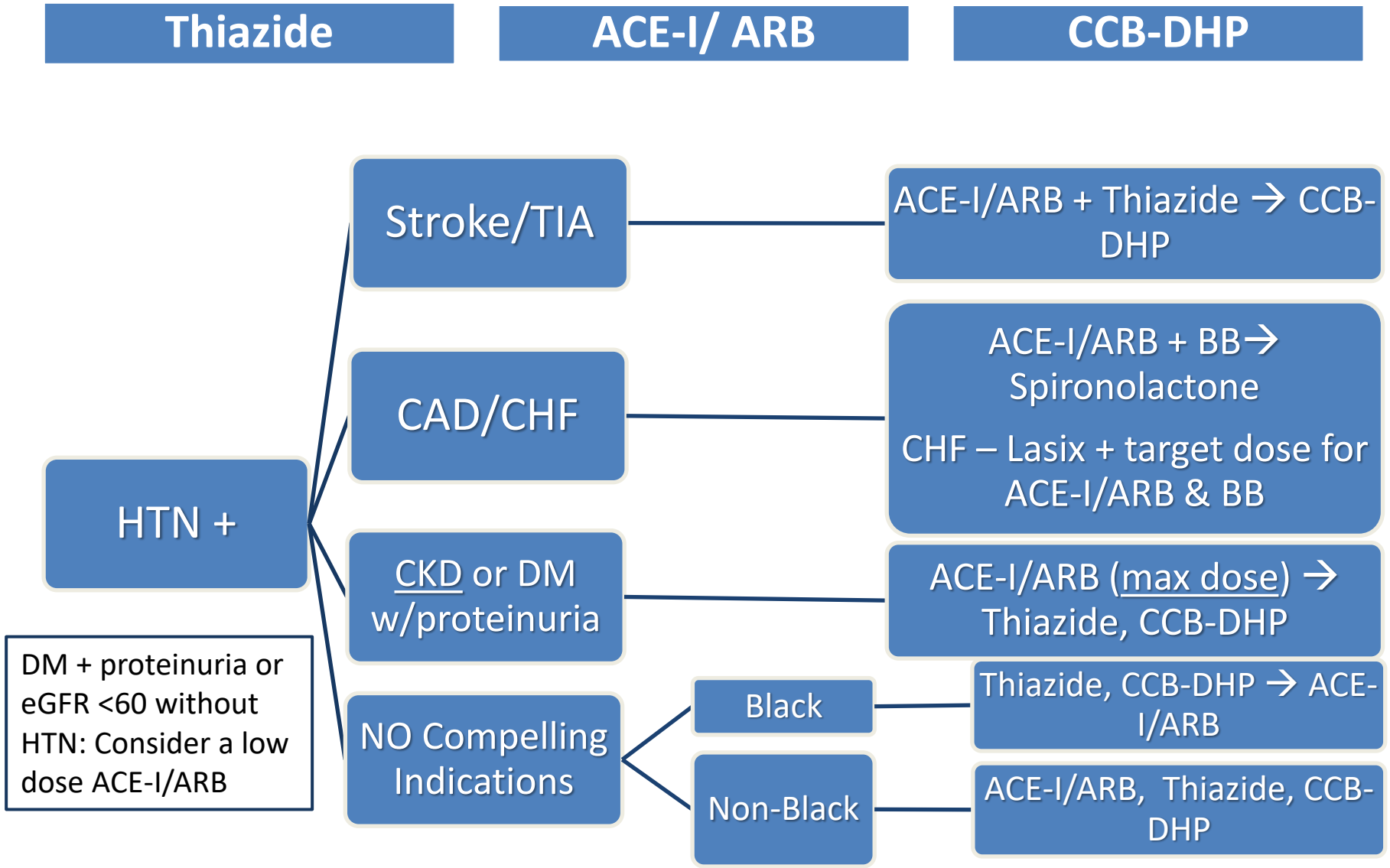
Start one agent

Initial BP >150/90 mmHg

↓

Start two agents

Treatment Recommendations



Remaining Classes NOT Recommended

- **Beta blockers**
  - Fatigue, ↓ exercice tolerance, depression, sexual dysfunction, increased DM risk
- **Alpha$_1$ blockers**
  - ALLHAT trial: 25%↑ in CV events
- **Central alpha$_2$ adrenergic agonists**
  - Sedation/falls, TID dosing, Rebound HTN
- **Direct vasodilators**
  - Orthostatic hypotension, QID dosing, Reflex tachycardia
- **Non-DHP CCB**
  - Heart block, HF exacerbation
- **Loop diuretics**
  - Minimal effect on BP, dehydration, electrolytes imbalance

Lifestyle Modification to Manage Hypertension

Modification	Recommendation	Approximate SBP reduction
Weight reduction	Maintain normal body weight (body mass index 18.5 to 24.9 kg/m^2)	5 to 20 mmHg/10 kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8 to 14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2 to 8 mmHg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week).	4 to 9 mmHg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter-weight persons.	2 to 4 mmHg

Patient Case #3

- A 55-year-old patient comes in for blood pressure screening. The patient reports no significant past medical history (i.e., diabetes). Systolic blood pressure is 148 and 149, and diastolic blood pressure is 92 and 93 after two separate readings.

  - Thiazide and lifestyle modifications
  - Thiazide and ACEI
  - No treatment warranted
  - β-blocker
  - Thiazide, β-blocker, and ACEI

Smoking

“No Safe Level of Smoking”

- 141 cohort studies
- Smoking just one cigarette per day can increase risk of stroke and coronary heart disease
- Smoking 1 cigarette per day compared to 20 cigarettes per day:
  - 31-46% of excess relative risk for CHD
  - 34-41% of excess relative risk of stroke

Smoking Cessation

- Identify smoking triggers
  - Cravings, ritual, after meals, with drinks, driving
- Determine plan to “de-link” smoking from the trigger
- Break smoking habits
  - Smoke with non-dominant hand
  - Switch cigarette brands
  - Postpone lighting of first cigarette by 1 hour
  - Substitute/delay each cigarette with gum, activity, etc.

My smoking cessation workbook. US Department of Veterans Affairs. Retrieved October 10,2015 from www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2827

Treatment Recommendations

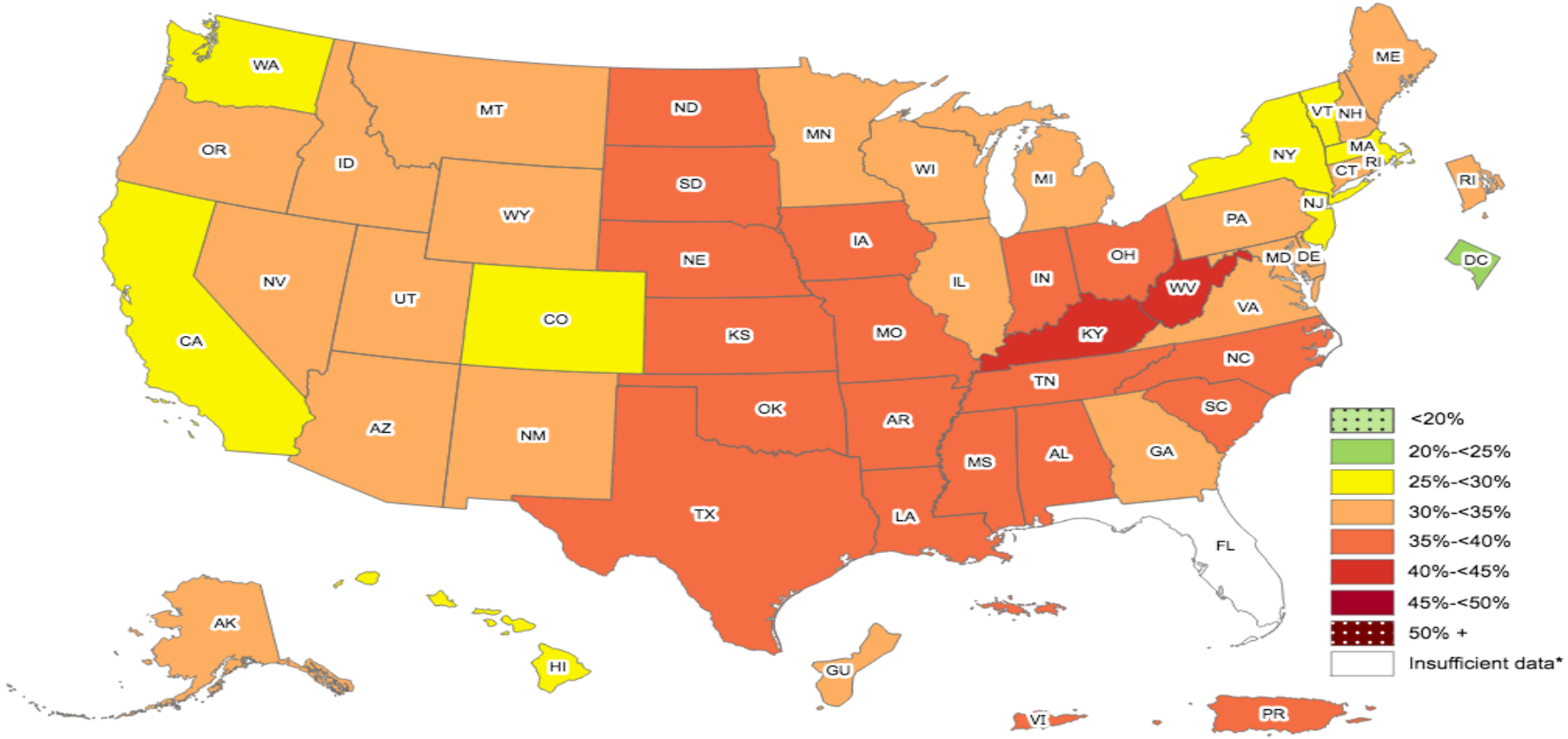
- Chantix (varenicline)
- Dual Nicotine Replacement Therapy (NRT)
- Zyban (bupropion SR) + NRT

Drug	Dosage form	Dosages	Clinical pearls
Nicoderm	Patch	21 mg for >10 CPD; 14 mg for <10 CPD	Hairless site; Rotate sites; Insomnia
Commit	Lozenge	4 mg if first tobacco use is ≤30 min after waking; 2 mg if first tobacco use is >30 min after waking; maximum of 20 lozenges or 24 pieces of gum/d. Chew and park gum	Park; N/V, hiccups Avoid food or beverages 15 min before and after use
Nicorette	Gum		Chew and park; Mouth soreness
Zyban (Bupropion SR)	Tablet	150 mg SR once daily for 3 days, increase to 150 mg SR twice daily for 7-12 weeks	Begin **1 week before quit date** SE: dry mouth, dizziness, headaches, insomnia **Contraindications**: history of seizure, use of MAO-Is within last 14 days, bipolar disorder, eating disorders
Chantix (Varenicline)	Tablet	Days 1-3: 0.5 mg once daily, days 4-7: 0.5 mg twice daily, then 1 mg twice daily	**Begin 1 week before quit date** SE: N/V, headache, insomnia, colored dreams

Patient Case #4

- A 38 year old female who presents for yearly annual checkup. Her past medical history is significant for hyperlipidemia, hypertension, and epilepsy. She is a current smoker and drinks socially. She currently takes atorvastatin 40mg daily, lisinopril 40mg daily, and levetiracetam 1000mg twice daily. After discussion with her primary care provider, she agrees to undergo an intensive smoking cessation program including counseling. Which of the following agents would be contraindicated for her smoking cessation?
  - A. Bupropion
  - B. Nicotine gum
  - C. Nicotine patches
  - D. Varenicline

Obesity Map 2022: Mean BMI

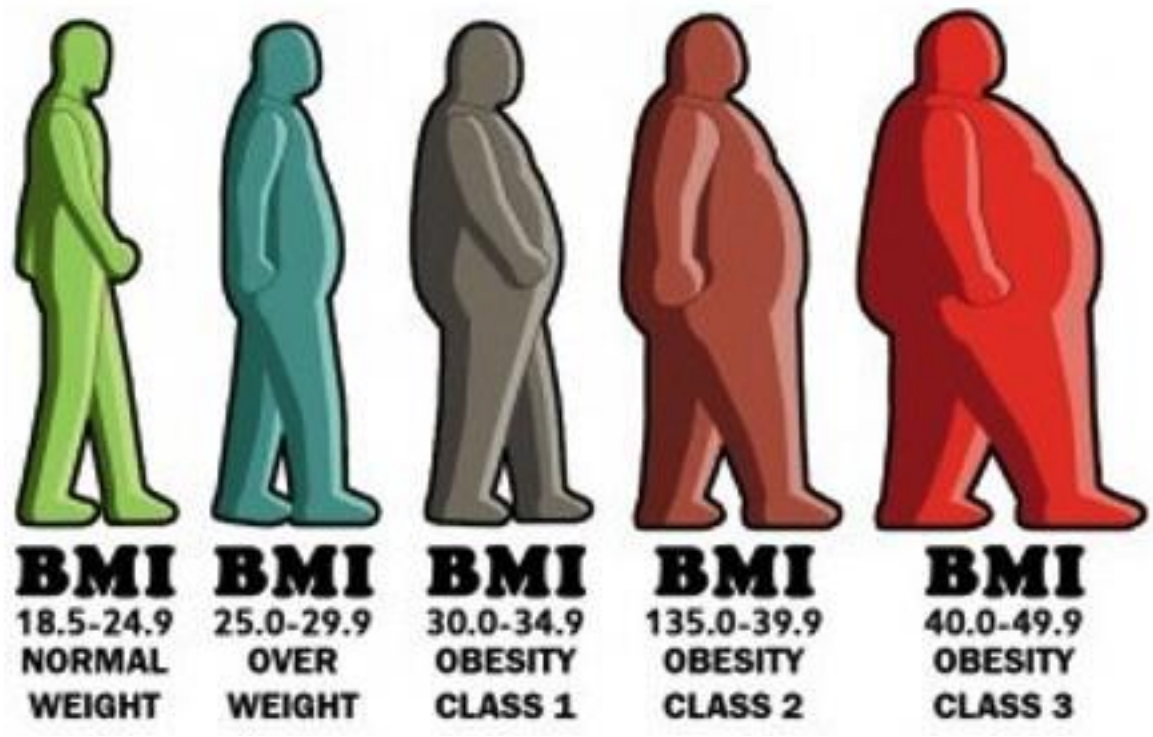


Centers for Disease Control and Prevention. Overweight & obesity. Available at: https://www.cdc.gov/obesity/index.html (Accessed on September 06, 2022).

What is Obesity?

- Excessive fat accumulation that presents a risk to health
  - Relates to increase in weight-for-height
- The most common method of measuring obesity is the

Body Mass Index (BMI)



https://healthylife.werindia.com/nutrition/bmi

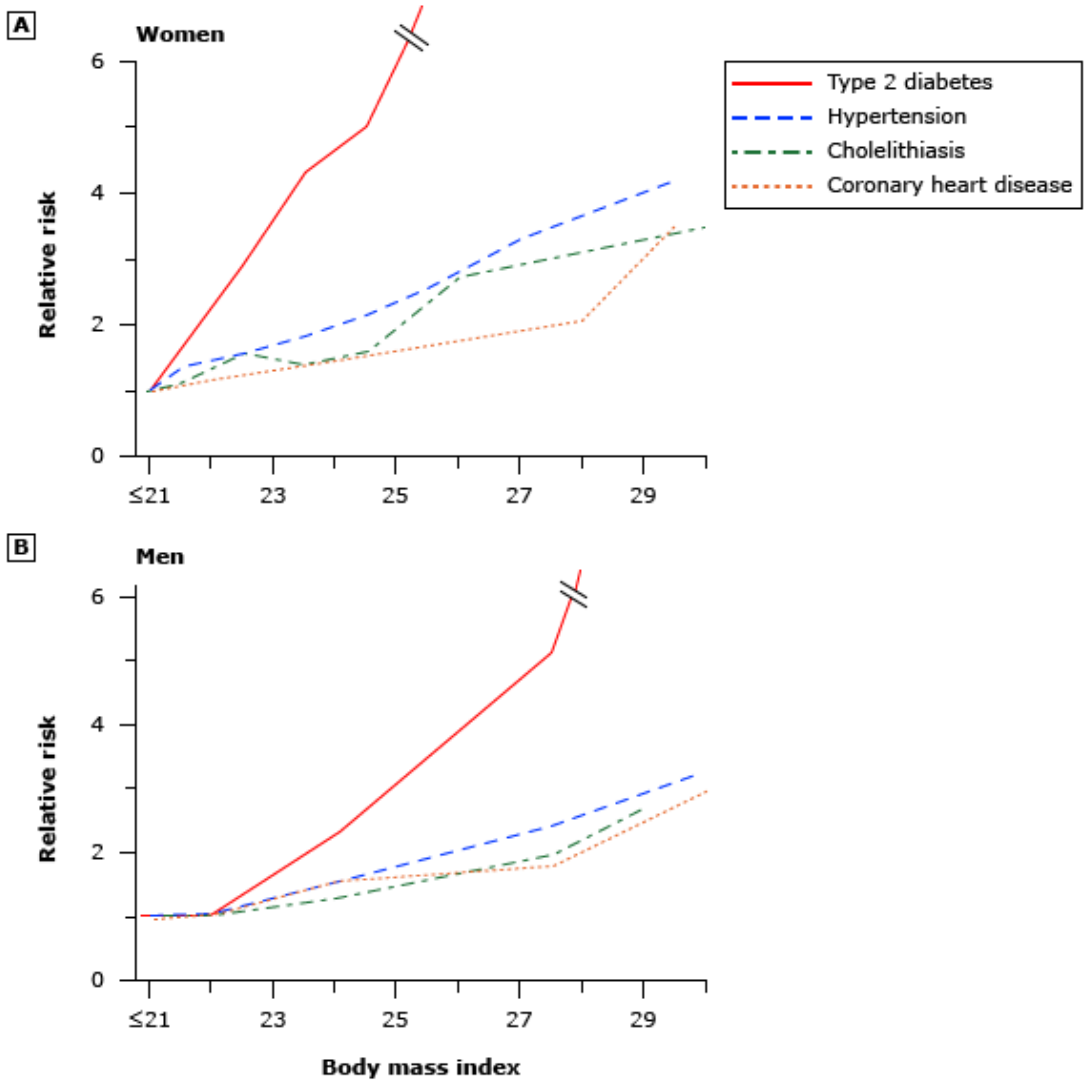
Drivers of Obesity

- Genetics
- Environment
- Excessive Energy Intake
- Medications
  - Antipsychotics

	Weight gain	Glucose abnormalities
Second-generation agents		
Aripiprazole	+	+
Asenapine	++	++
Brexpiprazole	+	+
Cariprazine	++	++
Clozapine	+++	+++
Iloperidone	++	++
Lumateperone	+	+
Lurasidone	+	++
Olanzapine	+++	+++
Paliperidone	++	+
Pimavanserin	-	+
Quetiapine	++	++
Risperidone	++	++
Ziprasidone	+	+

Medical Complications of Obesity

- Hypertension
- Stroke
- T2DM
- Metabolic syndrome
- CV mortality
- Cancer-endometrial, breast, prostate etc.
- Osteoarthritis
- Sleep apnea



Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. N Engl J Med 1999; 341:427.

Treatment Recommendations

- Weight Management
  - To see health benefits from weight loss need to lose 5-10% of body weight
  - 7-10% weight reduction decreases Type 2 diabetes risk by 58%
  - Calories count
    - **calories in < calories out**
  - Exercise
  - For weight loss it is recommended to exercise at moderate intensity 1 hour a day and for maintenance 30 min 5 times a week
- Pharmacotherapy
- Surgery
  - Bariatric surgery
  - Liposuction

Treatment Recommendations

Medication	Avg Wt Loss	MOA	AEs
Phentermine (Adipex-P), Phendimetrazine (Bontril), Benzphetamine (Regimex), Diethylpropion	5%	Adrenergic	Tachycardia, HTN, dependence/withdrawal CS-IV
Phentermine / Topiramate (Qsymia)	10%	Adrenergic, CNS	Tachycardia, HTN + neuropathy CS-IV REMS*
Lorcaserin (Belviq)	3.5%	$5HT_{2C}$	Dizziness, fatigue CS-IV
Bupropion / Naltrexone (Contrave)	4.5%	CNS, Opioid antagonism	Seizures, mood changes
Liraglutide (Saxenda)	7%	GLP-1	Nausea
Orlistat (Alli, Xenical)	3%	Lipase inhibitor	Steatorrhea, incontinence

Summary

- Diabetes
  - Cardiovascular disease (CVD), is the number one cause of death in people living with diabetes.
  - First-line therapy depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification.
- Dyslipidemia
  - At least a moderate-intensity statin should be started in patients with T2DM
- Hypertension
  - Goal: <130/80 mmHg
  - Thiazides, ACE-I/ARB, & CCB-DHP are recommended as first-line
- Smoking
  - Encourage smoking cessation during each visit
- Obesity
  - Lifestyle modifications are more effective for long term weight loss

References

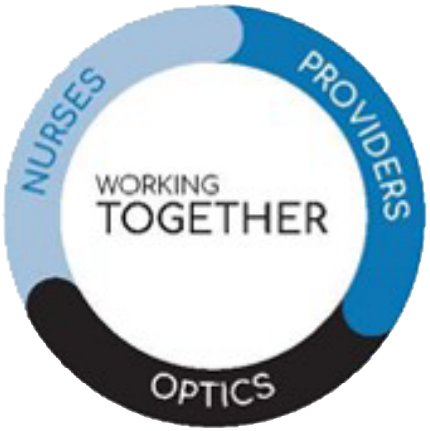
- *Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int 2021; 99:S1.*
- *Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018; 71:e13.*
- Hackshaw Allan, Morris Joan K, Boniface Sadie, Tang Jin-Ling, Milenković Dušan. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports *BMJ* 2018; 360 :j5855
- My smoking cessation workbook. US Department of Veterans Affairs. Retrieved October 10,2015 from www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2827
- Shah et al J AM Pharm Assoc 2008;48(5)659-65 Package Insert
- Benowitz NL, Pipe A, West R, et al. Cardiovascular Safety of Varenicline, Bupropion, and Nicotine Patch in Smokers: A Randomized Clinical Trial. *JAMA Intern Med.* 2018;178(5):622–631. doi:10.1001/jamainternmed.2018.0397
- Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. N Engl J Med 1999; 341:427.
- Centers for Disease Control and Prevention. Overweight & obesity. Available at: https://www.cdc.gov/obesity/index.html (Accessed on September 06, 2022).
- Grundy SM. Et all. Definition of metabolic syndrome: report of the National, Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation. 2004;109:433-438
- Alexander, C. NCEP-Defined Metabolic Syndrome, Diabetes, and Prevalence of Coronary Heart Disease Amoung NHANES III Participants Age 50 Years and Older. Diabetes May 2003 vol. 52 no. 5 1210-1214

OPTICS

Office of **P**harmacy **T**herapeutics
and **I**ntegrated **C**linical **S**ervices

Nancy Chia, Pharm D, MBA

- **Clinical Pharmacist**
- **PGY-1 Residency Completed**



1.800.882.6337 x1834 OPTICS@diamondpharmacy.com
Fax: 724.599.3570

A DIVISION OF:
DIAMOND
PHARMACY SERVICES