Diagnosing & Delivering News of Cardiometabolic Disease Diagnosis

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Disclosures

- Advisory Board for: AstraZeneca, Amarin, Amgen, Bayer, Boehringer Ingelheim, Esperion, Novartis, Novo Nordisk, Pfizer.
- Educational talks (not promotional) for: Edwards, Medtronic

Learning Objectives

- Recognize the diagnosis criteria for cardiometabolic disease
- Discuss the diagnosis of obesity, pre-diabetes mellitus, diabetes, hypertension, and hyperlipidemia diagnosis with patients.
- Identify ASCVD risk and discuss it with patients.

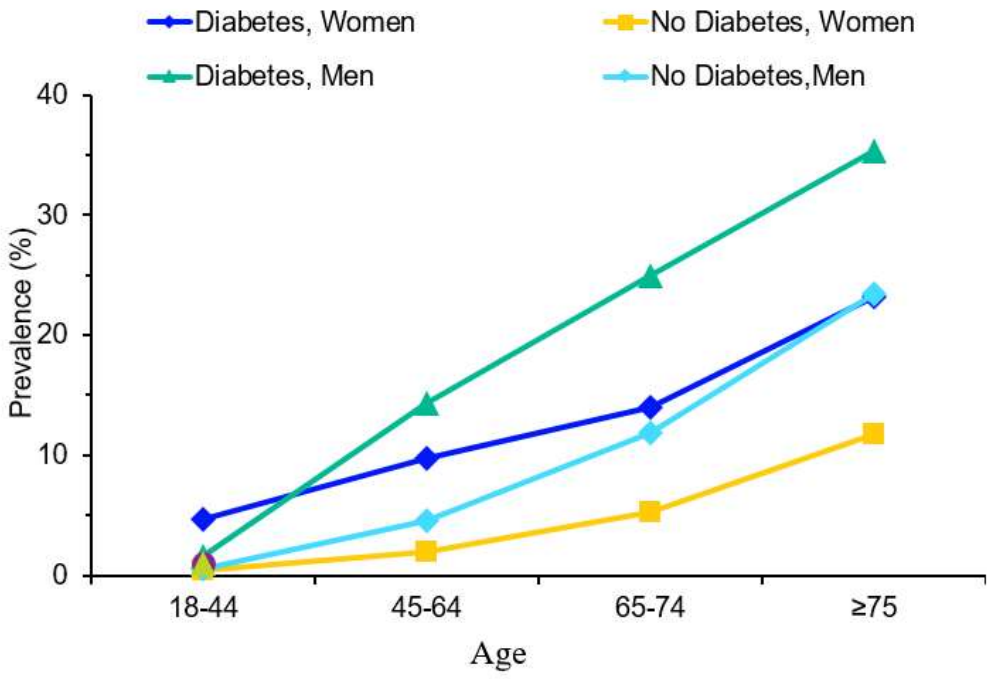
CV Risk & T2D

- **Heart disease** rates among adults with diabetes are **2 to 4 times** higher than rates for adults without diabetes
- The rate of CV death is increased **by 50%** in those with diabetes
- Diabetes increases the risk of **stroke**, with RR ranging from a **1.8- to 6-fold** increased risk
- Men and women ≥50 years of age with diabetes live an average of 7.5 and 8.2 years less, respectively, than their nondiabetic equivalents

ACS = acute coronary syndrome; HF = heart failure; RR = relative risk.
Go AS, et al. *Circulation.* 2014;129(3):e28-e292; Franco OH, et al. *Arch Intern Med.* 2007;167(11):1145-1151; Malmberg K, et al. *Circulation.* 2000;102(9):1014-1019.

Figure 18.2

Prevalence of Coronary Heart Disease by Diabetes Status, Sex and Age, U.S. 2019-2020



Source: 2019-2020 National Health Interview Survey

Kalyani R…**Michos ED**. Chapter 18 Heart Disease. *In* Diabetes in America. 2022; in press

Growing Prevalence of T2D in the United States

- The prevalence of diabetes is rapidly growing
- An estimated **37.3 million** Americans are living with diabetes (11% of US population)
  - That's more than 1 in 10 (11.3%) of US adults
  - More than 1 in 5 (23%) don't know they have diabetes
- By 2030, the prevalence is estimated to rise to **54.9 million!**

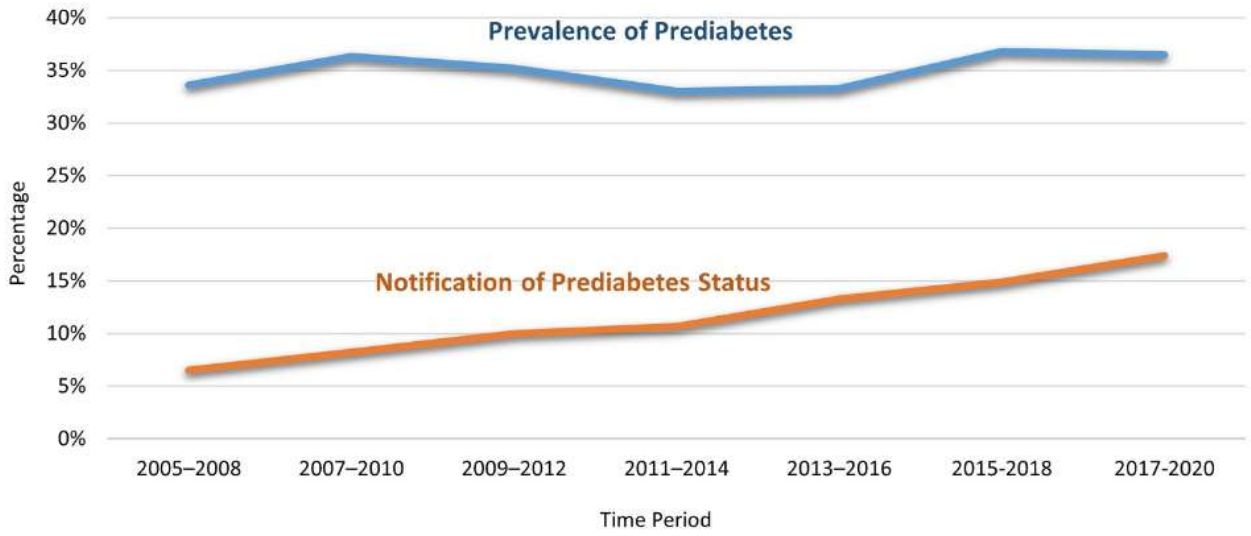
54.9 Million

2030

CDC National Diabetes Statistics Report 2020
image: Flaticon.com

Growing Prevalence of T2D in the United States

Figure 8. National Trends in Prevalence and Notification by a Health Professional of Prediabetes Among US Adults Aged 18 Years or Older, 2005–2008 to 2017–2020



Notes: Percentages are age-adjusted to the 2000 US Census standard population. Notification of prediabetes status was based on self-report and estimated only for adults with prediabetes. Prediabetes was defined as fasting plasma glucose values of 100–125 mg/dL or hemoglobin A1C values of 5.7%–6.4%. Time periods overlap and are moving averages, with two survey periods each. Figure adapted from CDC's *National Diabetes Statistics Report*.
Data source: National Health and Nutrition Examination Survey, Centers for Disease Control and Prevention

- CDC estimates that **96 million**—or more than **1 in 3**—US adults 18 or older had prediabetes in 2019.
  - over 37 million adults aged 45 to 64
  - over 26 million adults 65 or older.
  - A higher percentage of men (41.9%) had prediabetes than women (34.3%).
- More than 8 out of 10 adults with prediabetes don't know they have it.

Diagnosis of Prediabetes and Diabetes (American Diabetes Association)

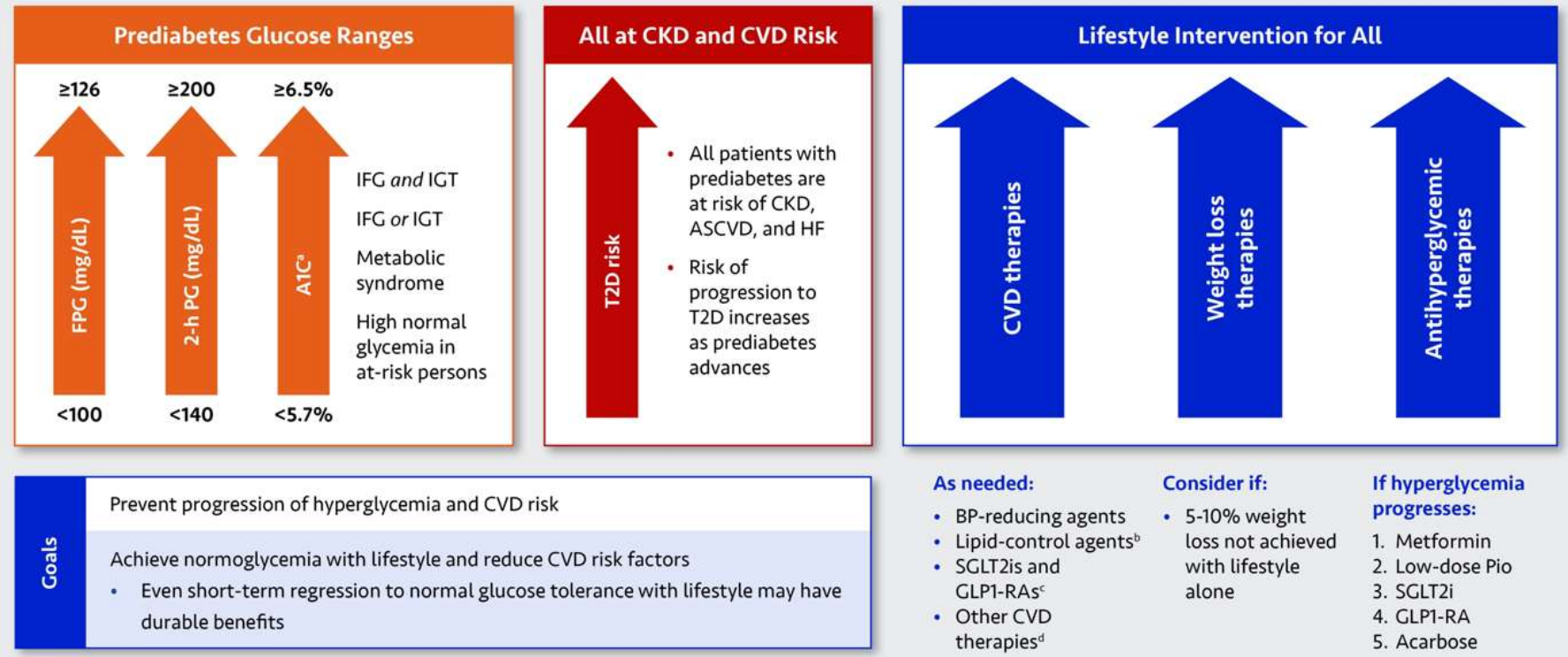
Prediabetes Diagnostic Criteria		
Fasting Plasma Glucose	2 hr PG 75 g OGTT	A1c
100-125 mg/dL	140-199 mg/dL	5.7-6.4%
Diabetes Diagnostic Criteria		
Fasting Plasma Glucose	2 hr PG 75 g OGTT	A1c
≥126 mg/dL	≥200 mg/dL	≥6.5
Or Random PG ≥200 mg/dL + hyperglycemic symptoms		

PG = plasma glucose
OGTT = oral glucose tolerance test

Hyperglycemic symptoms:
- Polydipsia
- Polyuria
- Polyphagia

American Diabetes Association. https://diabetes.org/diabetes/a1c/diagnosis

Spectrum of Glycemic Risk

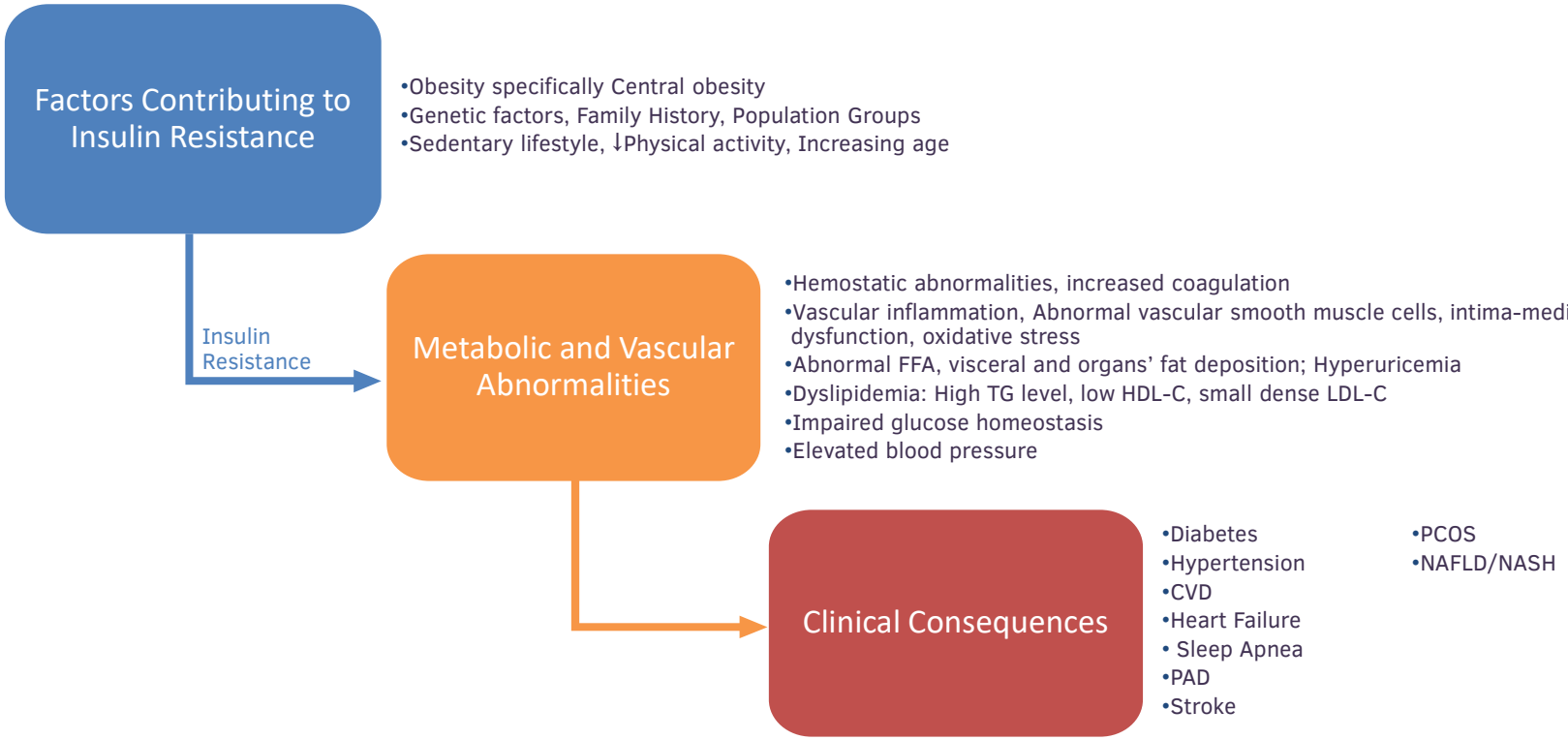


A1C = hemoglobin A1C; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CKD = chronic kidney disease; CVD = cardiovascular disease; FPG = fasting plasma glucose; GLP1-RA = glucagon-like peptide 1 receptor agonists; HF = heart failure; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; MRA = mineralcorticoid receptor agonist; PG = plasma glucose; Pio = pioglitazone; SGLT2i = sodium glucose cotransporter 2 inhibitors; T2D = type 2 diabetes.

[a] Caution with A1C diagnosis of prediabetes in African American, Latinx, and other ethnic groups.
[b] CVD benefit from statins more important than potential A1C increases.
[c] Trials with GLP1-RAs and SGLT2is ongoing.
[d] Antiplatelet therapies, MRAs, Pio 30 mg, etc.

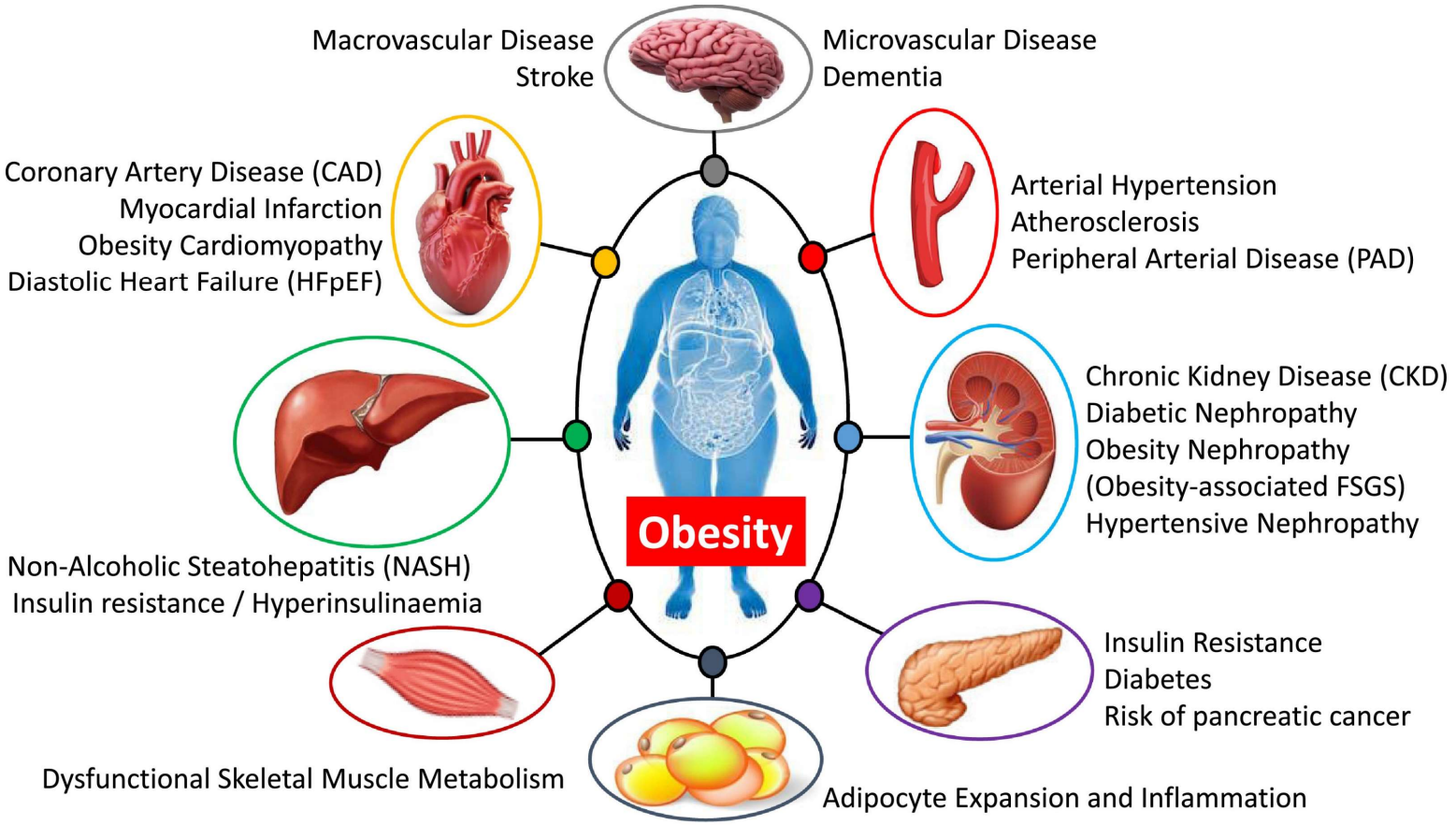
Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

Clinical Consequences of Insulin Resistance



CVD = cardiovascular disease; FFA=free fatty acids; NAFLD = nonalcoholic fatty liver disease; NASH = non-alcoholic steatohepatitis; PCOS = polycystic ovary syndrome; PVD = primary vascular dysregulation; TG = triglyceride. Kendall DM, Harmel AP. *Am J Manag Care.* 2002;8:S635-S653; Aroor AR, et al. *Heart Fail Clin.* 2012:8(4):609-617.

Long-term clinical consequences of obesity on metabolic and cardiovascular function in adults



Cardillo C et al. Endocrine and Metabolic Science 2021

Metabolic Syndrome

Waist circumference ≥40 inches (men); ≥35inches (women)

Fasting glucose ≥100 mg/dl

Triglycerides ≥150 mg/dl

HDL < 40 mg/dl (men); < 50 mg/dl (women)

SBP ≥130 mmHg; DBP ≥85mmHg

CardioSmart Patient Info Tools
https://www.cardiosmart.org/assets/infographic/metabolic-syndrome

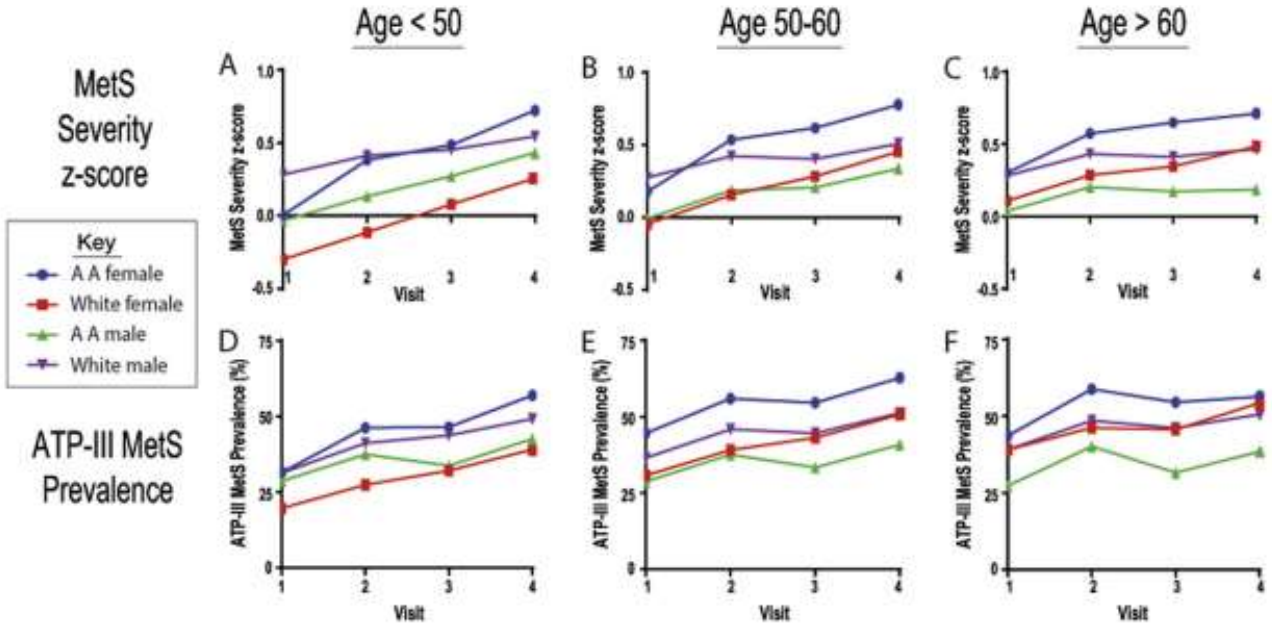
Metabolic Syndrome: Addressing Diagnostic Components of Metabolic Syndrome is Not Enough!

- Additional pathophysiologic features of metabolic syndrome contribute to ASCVD risk:
  - *Inflammation*
  - *Endothelial Dysfunction*
  - *Small, dense LDL particles*
  - *Prothrombosis*
- Lifestyle modification needed to address all pathophysiologic aspects of metabolic syndrome

Metabolic Syndrome

- Metabolic syndrome present in over 1/3 of US adults (>50% of adults >65 years)
  - Likely underrecognized in clinical practice due to inadequate screening
- Associated Risk:
  - 1.5-2 times higher ASCVD
  - 5 times higher DM

If no intervention, syndrome tends to worsen over time:



Gami AS et al. J AM Coll Cardiol. 2007 Jan 30;49(4):403-14.
Galassi A et al. Am J Med. 2006 Oct;119(10):812-9.
Vishnu A et al. Atherosclerosis. 2015 Nov; 243(1): 278–285.

Why is it a syndrome?

- **Syndrome** – a group of signs or symptoms that occur together and characterize a particular abnormality[1]
  - Greek: “syn” – together, “drome” – same road

Metabolic Syndrome

- Constellation of major risk factors, life-habit risk factors and emerging risk factors
- Obesity as exacerbating factor but insulin resistance as causal
- Over-represented among populations with CHD
  - Strong association of obesity with CVD and T2D
- Clue is distinctive body-type with increased abdominal circumference (although some leaner men and women with abdominal obesity without increased waist)
- Metabolic factors have moderate correlation with each other (r=0.15-0.82)
  - But is it a “syndrome”?
- The value of focusing on metabolic syndrome as a concept is that small amounts of weight loss result in improvement not only in blood pressure, but also in abnormal glucose/lipids

1.Webster’s New Collegiate Dictionary

Healthy Lifestyle Can Reverse Metabolic Syndrome Abnormalities

- Mediterranean Diet adherence (meta-analysis of N > 500,000):
  - ↓ WC 0.42 cm
  - ↓ Triglycerides 6.1 mg/dl
  - ↑ HDL-C 1.2 mg/dl
  - ↓ SBP 2.4 mmHg
  - ↓ DBP 1.6 mmHg
  - ↓ Fasting glucose 3.9 mg/dl
  - ↓ MS incidence by 31%
- Metabolic benefits seen with other heart healthy diets

Aerobic Exercise Increases Likelihood of Improving Metabolic Abnormalities

Target	First Quintile (RC) (≤4.74)	Fifth Quintile (>24.63)	*P* Value for Trend
HbA_{1c} <6.5%	1 [Reference]	1.5 (0.8-2.9)	.13
HbA_{1c} reduction ≥0.5	1 [Reference]	4.6 (2.1-10.0)	.02
TG <150 mg/dL	1 [Reference]	1.4 (0.7-2.6)	.23
TC <175 mg/dL	1 [Reference]	1.7 (1.0-3.0)	.93
HDL-C >40 mg/dL	1 [Reference]	2.9 (1.4-6.0)	.30
LDL-C <100 mg/dL	1 [Reference]	2.0 (1.1-3.5)	.65
SBP <130 mm Hg	1 [Reference]	2.2 (1.1-4.4)	.05
DBP <80 mm Hg	1 [Reference]	1.6 (0.8-3.1)	.33
BMI reduction ≥1	1 [Reference]	3.1 (1.7-5.6)	<.001
Waist circumference reduction ≥5 cm	1 [Reference]	15.9 (5.9-43.2)	<.001

Kastorini CM et al. J Am Coll Cardiol. 2011 Mar 15;57(11):1299-313
Balducci S et al. Arch Intern Med. 2010 Nov 8;170(20):1794-803.

The Metabolic Syndrome

A useful clinical phenotype for communicating:

Very high risk for diabetes

Higher short-term risk for CVD

Very high lifetime risk for CVD

Mechanism of risk – lifestyle and genetics

Risk beyond expected by traditional risk factors

Talking to your patient about weight management

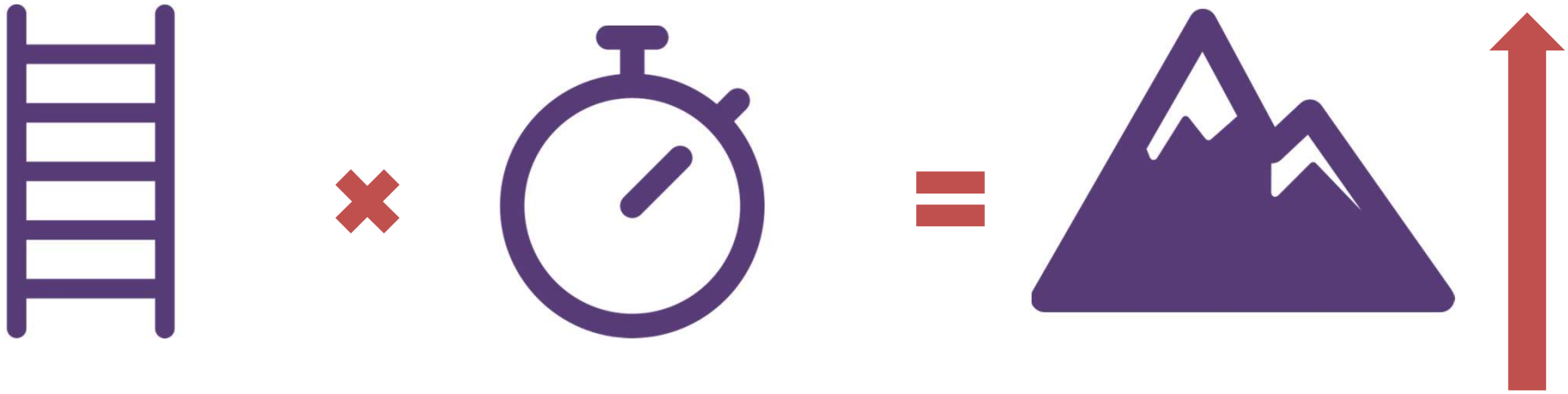
- Address your patient's main concerns for visit first
- Open discussion about weight in a respectful and non-judgmental way
- Obesity is a chronic health condition, that is far more complex than simply calories in and calories out.
- Ask patient's permission to discuss their weight
- Although obesity is a clinical term, research shows that this can be stigmatizing to patients. Preferred words "excess weight" or "elevated BMI".
  - Avoid terminology of morbid obesity.
- Express your concerns about the health risk associated with excess weight and how this is affecting the patient's own health
- Modest weight changes (5-10%) can improve health metrics
- When lifestyle changes have been tried and exhausted, there are new pharmacotherapies (GLP1-receptor agonists) than can help.
- The 5 As (**ask, assess, advise, agree, and assist**), developed for smoking cessation, can be adapted for obesity counseling

Cumulative Burden of ASCVD Risk Factors

Magnitude of Elevation

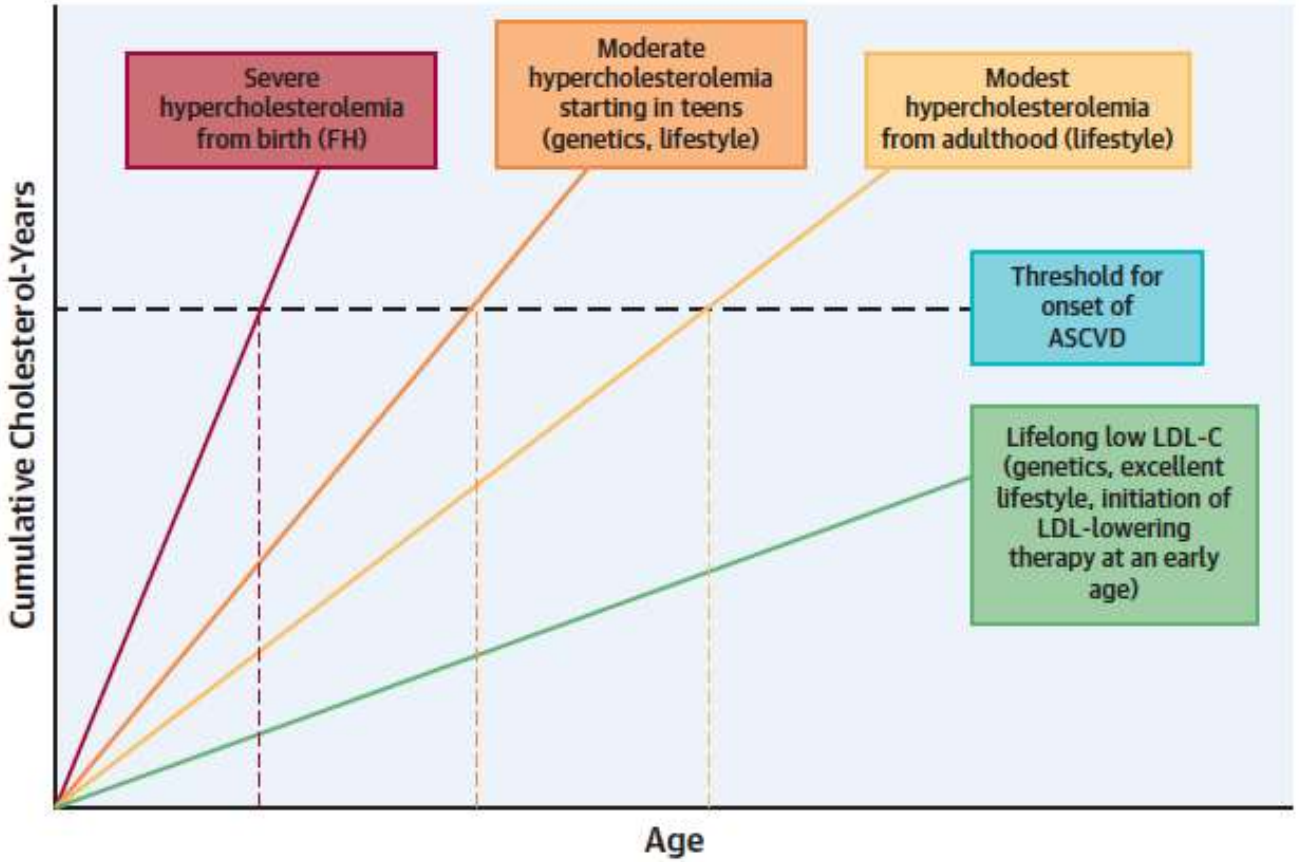
Duration of Elevation

Cumulative Risk



Icon source: flaticon.com

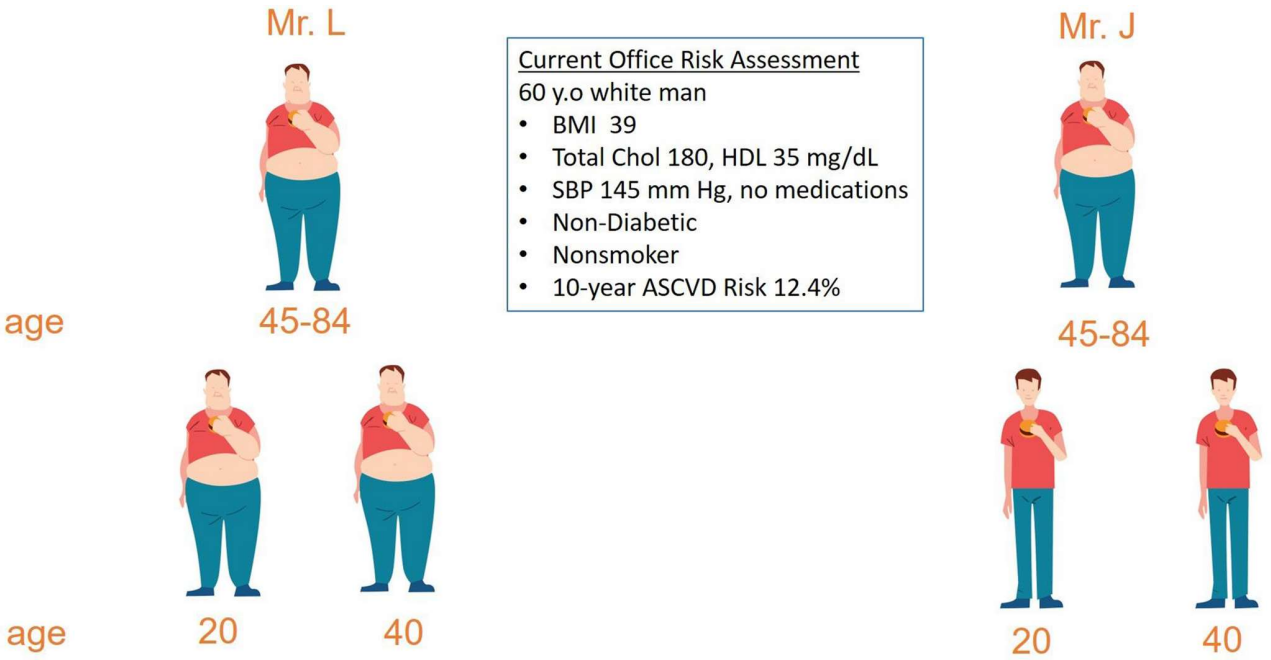
LDL-C "Pack Years": Cumulative LDL-C and ASCVD Risk



Shapiro MD, Bhatt DL. *J Am Coll Cardiol.* 2020;76(13):1517-1520.

BMI-years and incident HF

Central Illustration: Tale of 2 Patients



Fliotsos M…..**Michos ED**. Body Mass Index From Early-, Mid-, and Older-Adulthood and Risk of Heart Failure and Atherosclerotic Cardiovascular Disease: MESA, J Am Heart Assoc 2018; 7 (22): e009599

BMI-years and incident HF (MESA)

- Participant mean±SD age at the baseline examination was 62.2±10.2 years.
- Self reported weights at age 20 and 40 were asked
- Followup for incident HF, median followup 13 years

Even after adjusting for current BMI at baseline exam

Table 3. Incidence Rates and Adjusted Hazard Ratios (95% CI) for Incident Heart Failure Associated With BMI at Each Age Point

	N Events/Person-Year	IR (95% CI)*	Model 1†	Model 2‡	Model 3§
BMI at age 20 y, per 5 kg/m^2 higher‖	290/74 317	4.3 (3.8, 4.7)	1.44 (1.24, 1.67)¶	1.40 (1.20, 1.63)¶	1.27 (1.07, 1.50)¶
BMI at age 40 y, per 5 kg/m^2 higher‖	290/74 317	4.3 (3.8, 4.7)	1.53 (1.39, 1.70)¶	1.45 (1.29, 1.62)¶	1.36 (1.18, 1.57)¶
BMI at baseline, per 5 kg/m^2 higher	290/74 317	4.3 (3.8, 4.7)	1.43 (1.28, 1.60)¶	1.31 (1.16, 1.48)¶	
Time-varying BMI (v1–v5) per 5 kg/m^2 higher	284/73 643	3.9 (3.4, 4.3)	1.45 (1.30, 1.62)¶	1.34 (1.19, 1.51)¶	

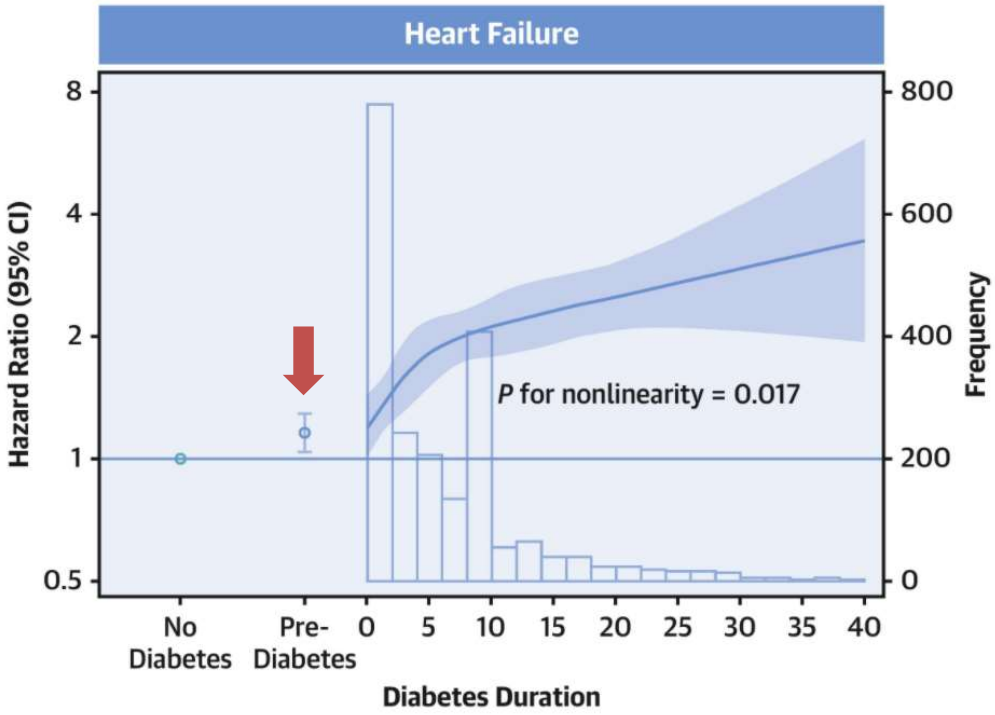
*IR: (95% CI) per 1000 person-y, adjusted for age, sex, race, and center.
† Model 1 (demographics and SES model): adjusted for age at baseline, sex, race/ethnicity, center, and education.
‡ Model 2 (+CVD risk factors): additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, HDL-C, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus.
§ Model 3 (for analyses of BMIs at age 20 and 40 y): additionally adjusted for BMI at MESA baseline

Self-reported lifetime weight is a low-tech tool easily utilized in any clinical encounter. Although subject to recall bias, self-reported weights may provide prognostic information about future HF risk, incremental to current BMI, in a multiethnic cohort of middle-aged to older adults.

Fliotsos M…..**Michos ED**. Body Mass Index From Early-, Mid-, and Older-Adulthood and Risk of Heart Failure and Atherosclerotic Cardiovascular Disease: MESA, J Am Heart Assoc 2018; 7 (22): e009599

Diabetes-years and incident HF (ARIC)

Central Illustration: Restricted Cubic Splines of the Diabetes Duration Association with Heart Failure Among Individuals with Diabetes



Echouffo-Tcheugui, J.B. et al. J Am Coll Cardiol HF. 2021;9(8):594-603

CV Risk Assessment. Why Assess Risk?

Rational for Absolute Risk Estimation

- Most important way to prevent CVD is to follow a healthy lifestyle throughout one's lifetime.

- When considering drug therapy, estimation of risk facilitates matching intensity of therapy to one's **absolute risk** to:
  - Maximize anticipated benefits of therapy
  - Minimize harms of over-treatment

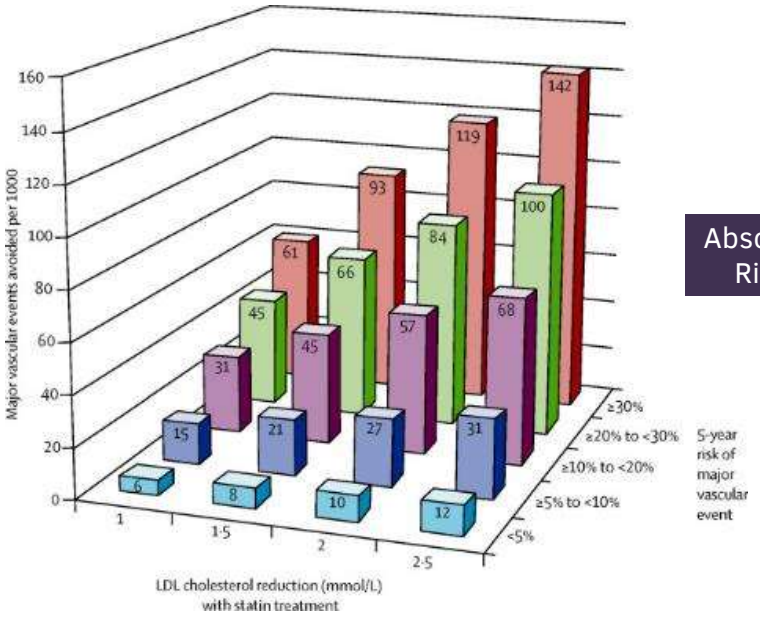
Icon source: flaticon.com

Why Assess Risk?

Rational for Absolute Risk Estimation

Cholesterol Treatment Trialists

Vascular events avoided



Absolute Risk

LDL-C Reduction

- Allows identification of patients at sufficient risk to merit treatment with higher likelihood of net individual and societal benefit
- Allows direct comparison of potential benefits and harms from drug therapy

CTT, Lancet 2012; Lloyd-Jones et al., Circ and JACC 2018

Icon source: flaticon.com

2019 ACC/AHA Guidelines on Primary Prevention Patients with Diabetes Mellitus

*No need to calculate 10-year ASCVD risk score

Recommendations for Adults with High Blood Cholesterol		
COR	**LOE**	**Recommendations**
I	A	In adults 40 to 75 years of age with diabetes*, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.
IIa	B-R	In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more.

Diabetes-specific risk enhancing factors

- Long duration
  - ≥10 years for T2DM
  - ≥20 years for type 1 DM
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 mL/min/1.73 m^2
- Retinopathy
- Neuropathy
- ABI <0.9

Arnett DK, Blumenthal RS,….**Michos ED**…et al. Circulation 2019

2019 ACC/AHA Guidelines on Primary Prevention of CVD

Assessment of 10-year ASCVD Risk

Recommendations for Assessment of Cardiovascular Risk		
COR	**LOE**	**Recommendations**
I	B-NR	For adults **40 to 75 years of age**, clinicians should routinely assess traditional cardiovascular risk factors and **calculate 10-year risk of ASCVD** by using the **pooled cohort equations (PCE)**.

Arnett DK, Blumenthal RS,....**Michos ED**...et al. Circulation 2019

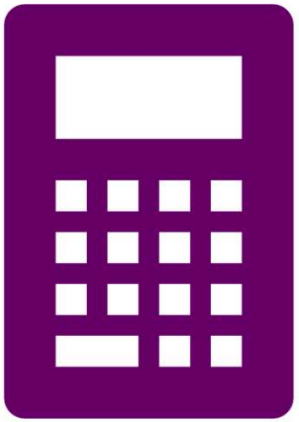
2019 ACC/AHA Primary Prevention Guidelines

Assessment of 10-year ASCVD Risk

Risk Factor	Units
Sex	M or F
Age	Years
Race	AA or WH
Total Cholesterol	mg/dL
HDL-Cholesterol	mg/dL
Systolic Blood Pressure	mm Hg
Treatment for Hypertension	Y or N
Diabetes	Y or N
Smoker	Y or N

AHA ASCVD Risk Calculator (online/app)http://static.heart.org/riskcalc/app/index.html#!/baseline-risk

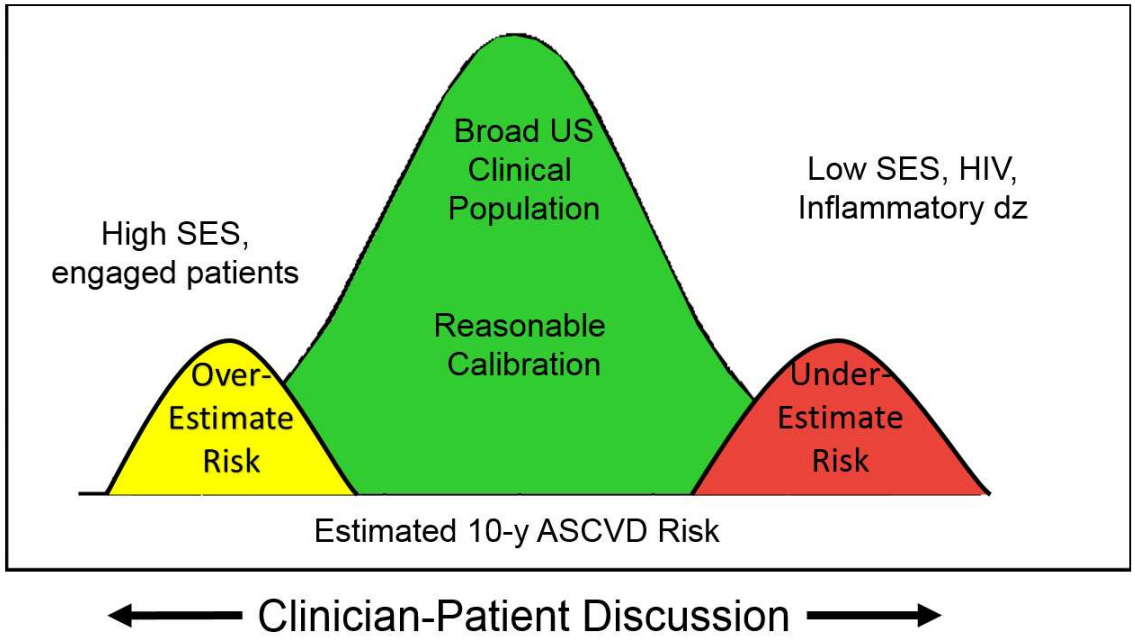
- Based on multiple cohorts; sex and race-specific
- Stroke included in addition to MI and CHD mortality



Goff DC et al. 2013 ACC/AHA Guideline on Assessment of Cardiovascular Risk. Circulation 2014;129(25 Suppl 2):S49-73.

2019 ACC/AHA Primary Prevention Guidelines

Performance of PCE in Diverse Populations



PCE: Pooled Cohort Equations; SES, socioeconomic status

Amin NP….**Michos ED**. Headed in the right direction but at risk for miscalculation: a critical appraisal of the 2013 ACC/AHA risk assessment guidelines. J Am Coll Cardiol 2014 Jul 1;63(25 Pt A):2789-94.

2019 ACC/AHA
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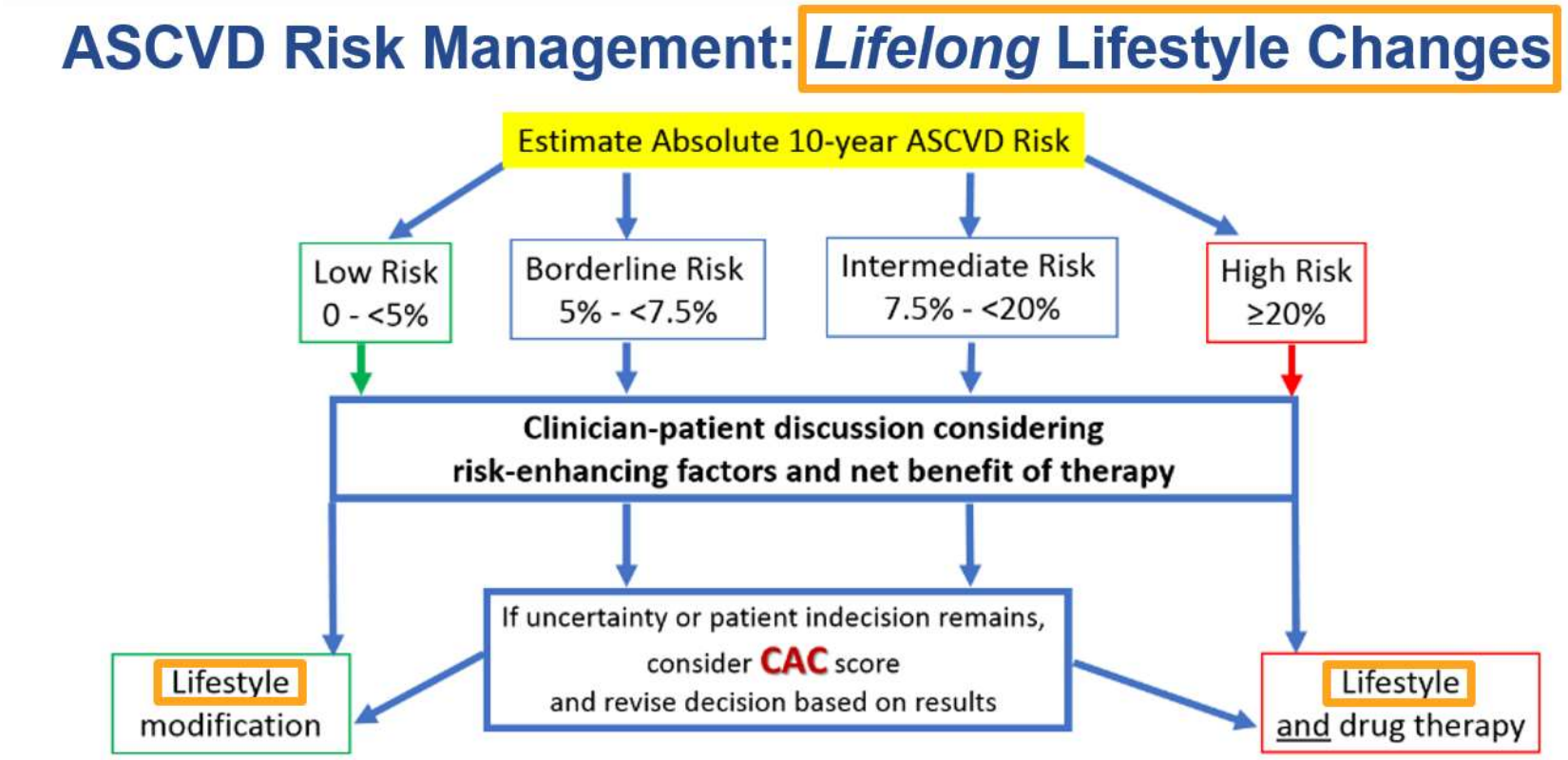
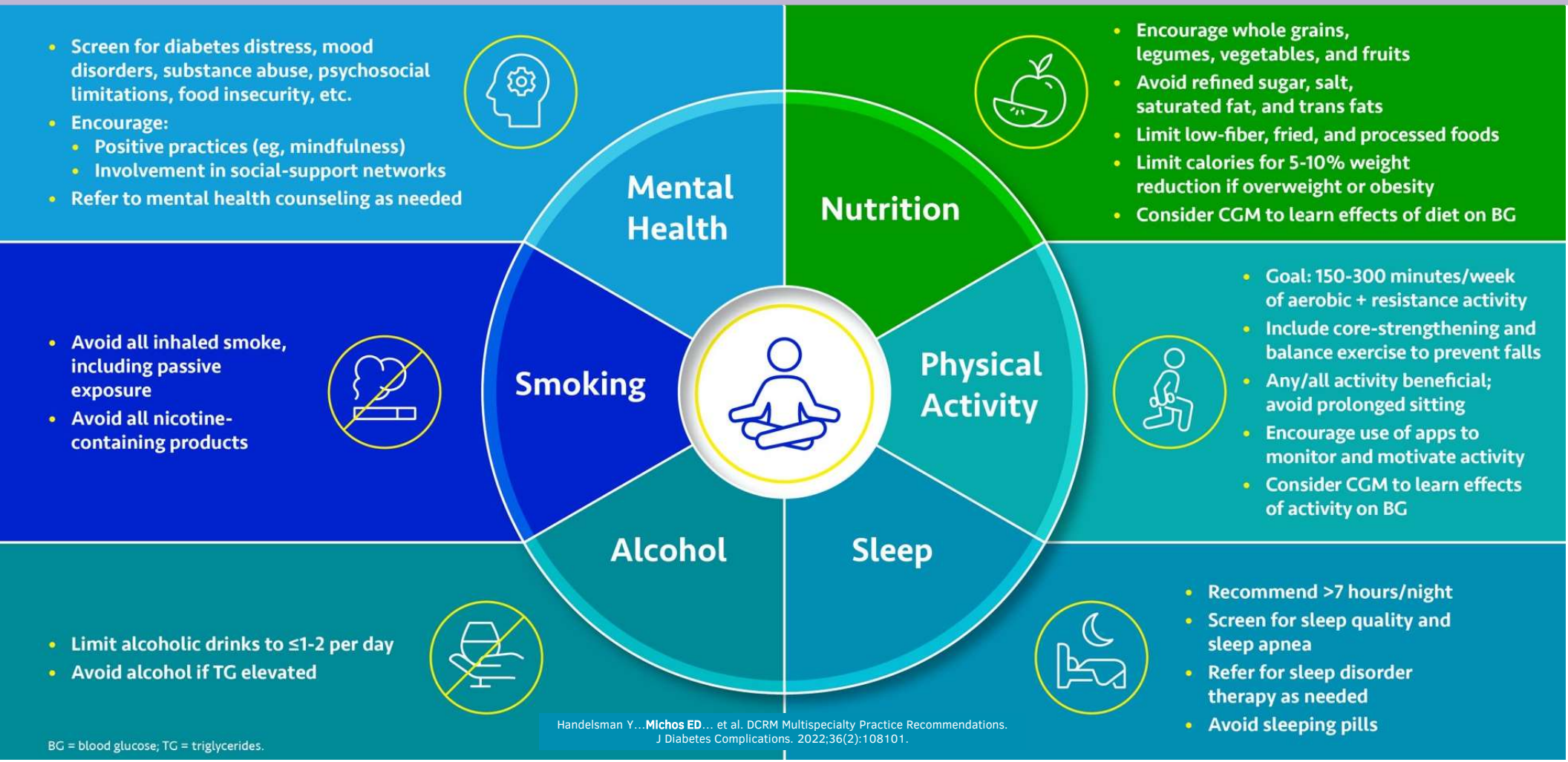


Arnett DK, Blumenthal RS,....**Michos ED**...et al. Circulation 2019

Elements of Lifestyle Therapy – Any Effort is Worthwhile



BG = blood glucose; TG = triglycerides.

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

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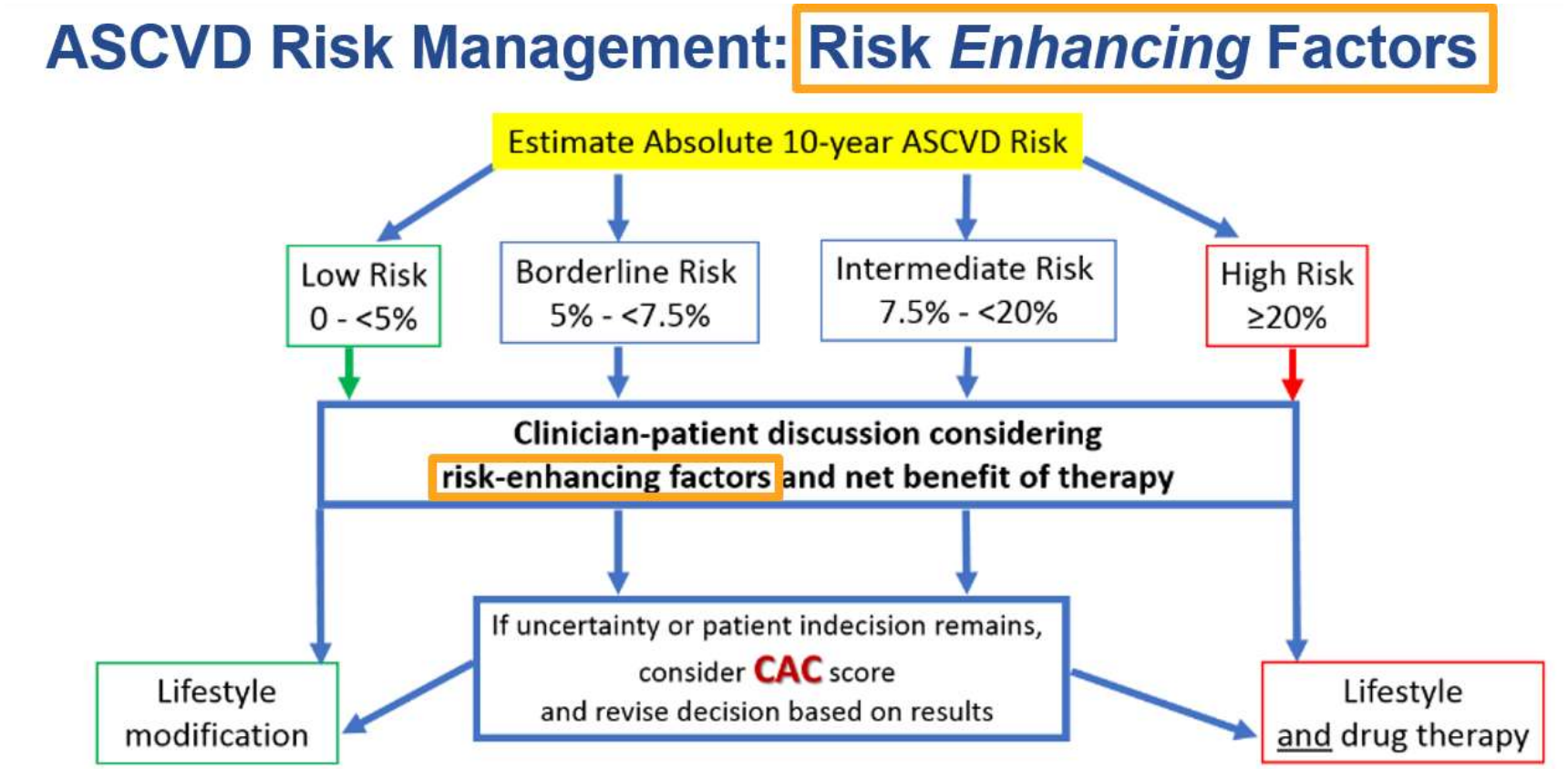
Primary Prevention Guidelines



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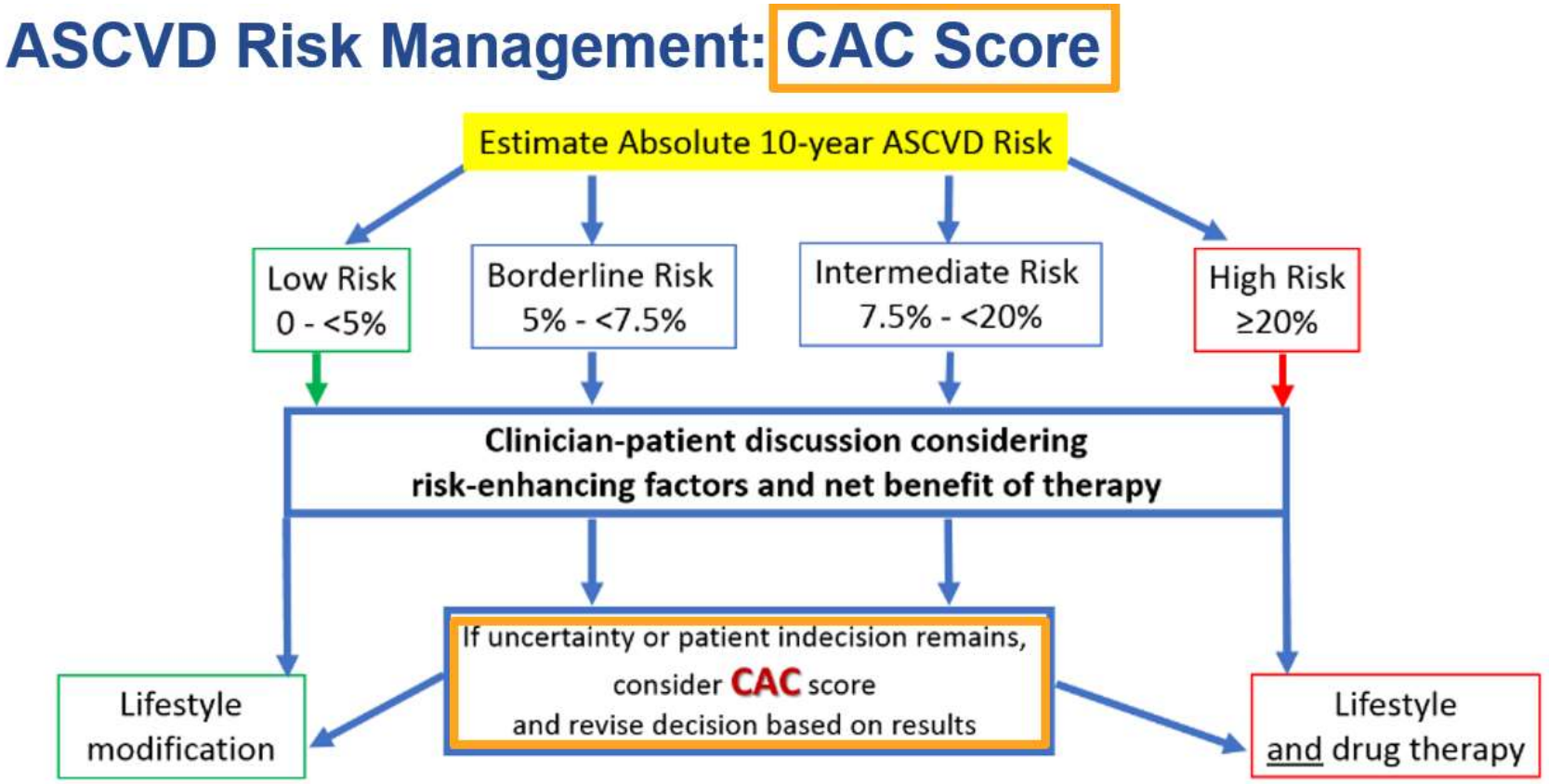
2019 ACC/AHA Primary Prevention Guidelines: Risk Enhancing Factors

- **History of premature menopause (before age 40) and history of pregnancy associated conditions that increase later ASCVD risk such as preeclampsia**
- **Family history of premature ASCVD (men, age <55 years; women, <65 years)**
- **Primary hypercholesterolemia** (LDL-C 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])
- **Metabolic syndrome** (**increased waist circumference** [by ethnically appropriate cutpoints], **elevated triglycerides [>150 mg/dL, nonfasting]**, **elevated blood pressure, elevated glucose**, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions,** such as psoriasis, RA, lupus, or HIV/AIDS
- **High-risk race/ethnicity** (eg, South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk:
- Persistently **elevated hypertriglycerides** (≥175 mg/dL, nonfasting);
- **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
- **Elevated Lp(a):** An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
- **Elevated apoB** (≥130 mg/dL): A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor.
- **ABI** *(*<0.9)

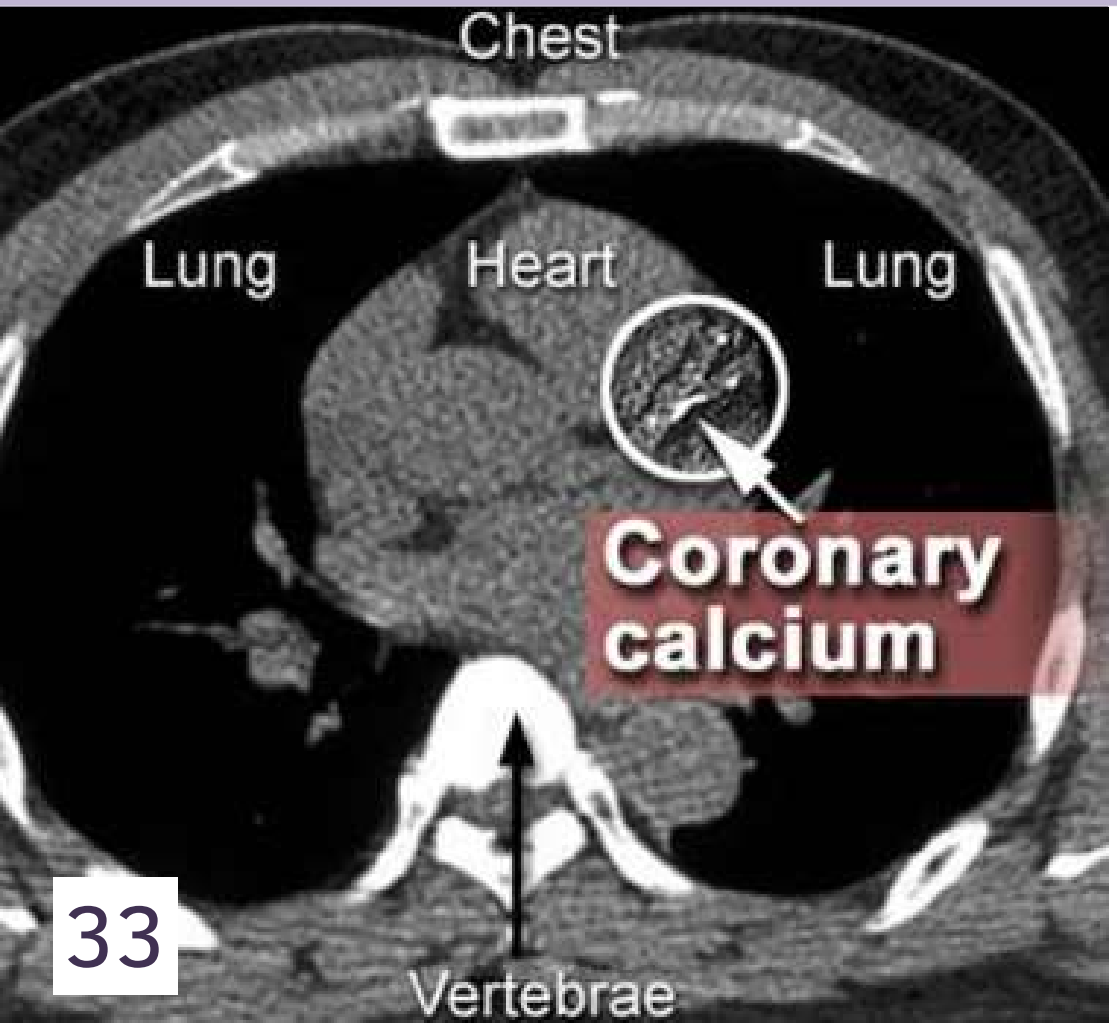
Arnett DK, Blumenthal RS,….**Michos ED**…et al. Circulation 2019

2019 ACC/AHA
Primary Prevention Guidelines



Arnett DK, Blumenthal RS,....**Michos ED**...et al. Circulation 2019

When Risk is Uncertain: Plaque Imaging May Help



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Coronary Artery Calcium (CAC) by non-contrast computed tomography (CT)

~1 mSv

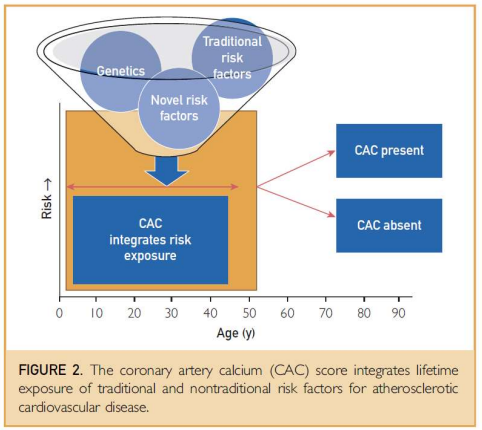


FIGURE 2. The coronary artery calcium (CAC) score integrates lifetime exposure of traditional and nontraditional risk factors for atherosclerotic cardiovascular disease.

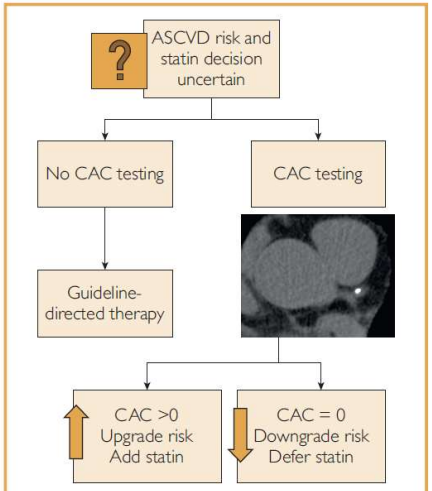
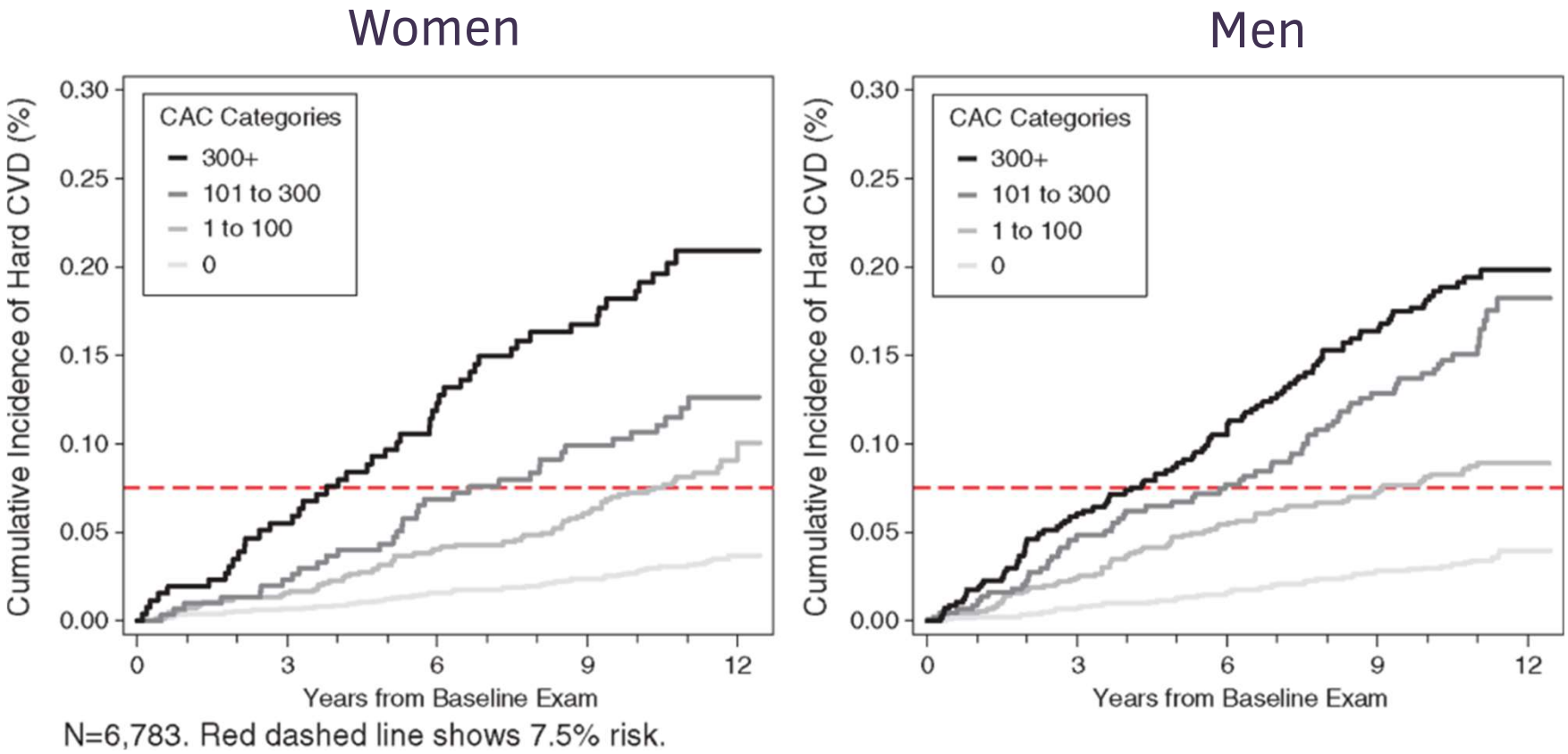


FIGURE 3. Coronary artery calcium (CAC) testing to guide the treatment decisions.

Michos ED et al. Mayo Clin Proc 2017 Dec;92(12):1831-1841.

10-yr ASCVD risk by CAC Score by Sex
Multi-Ethnic Study of Atherosclerosis (MESA)

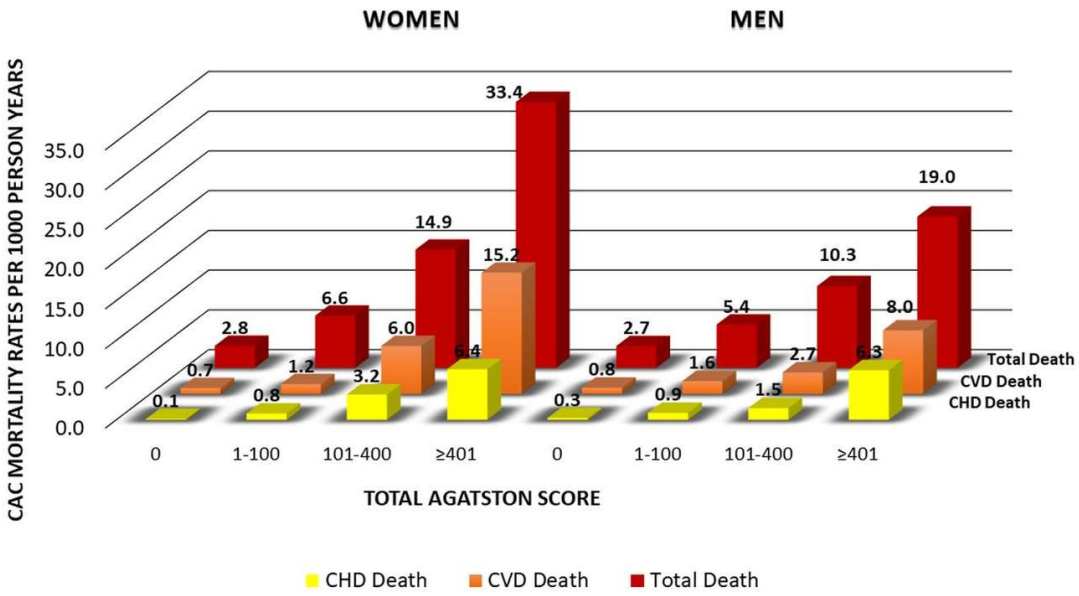


N=6,783. Red dashed line shows 7.5% risk.

Budoff MJ....**Michos ED**... et al. *E Heart J.* 2018;39:2401-2408.

Among patients with diabetes, greater CAC predicts total and CVD mortality more strongly in women

- CAC Consortium cohort
- 4,503 adults with diabetes (32.5% women) aged 21–93 years
- CAC >0 in 61.2% of women & 80.4% of men (interaction *P*=0.01).



	Total Mortality (Adjusted HR and 95% CI)	
	MEN	WOMEN
CAC=0	Ref	Ref
CAC 1-100	1.36 (0.83-2.24)	1.43 (0.81-2.56)
CAC 101-400	1.88 (1.15-3.09)	2.56 (1.45-4.53)
CAC >400	2.61 (1.61-4.24)	4.05 (2.33-7.04)
P-interaction by sex 0.01		

	CVD Mortality (Adjusted HR and 95% CI)	
	MEN	WOMEN
CAC=0	Ref	Ref
CAC 1-100	1.36 (0.54-3.45)	0.96 (0.29-3.21)
CAC 101-400	1.63 (0.64-4.14)	3.67 (1.30-10.38)
CAC >400	3.48 (1.44-8.37)	6.27 (2.27-17.28)
P-interaction by sex 0.04		

Wong ND et al. Diabetes Care 2020;43:2597-2606

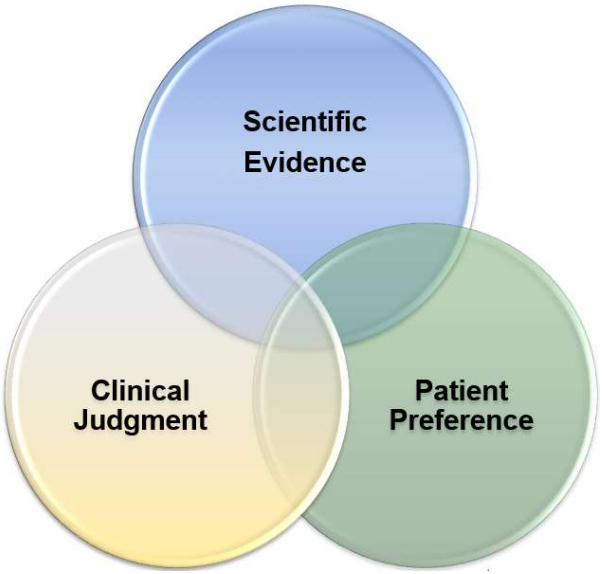
2019 ACC/AHA Primary Prevention Guidelines: Shared Decision Making

Clinician-Patient Risk Discussion

Initiating Treatment in Primary Prevention

Clinicians and patients should discuss:

1. Estimated 10-yr risk, major risk factors, & risk-enhancing factors
2. Potential ASCVD risk reduction benefits of lifestyle + drug therapy
3. Potential adverse effects, drug interactions, & costs
4. Patient Preferences & values in shared decision-making



Martin SS et al. Clinician-patient risk discussion for atherosclerotic cardiovascular disease prevention: importance to implementation of the 2013 ACC/AHA Guidelines. *J Am Coll Cardiol* 2015;65(13):1361-1368.

Elements of Patient Self-Management Education: A Clinician's Guide

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

Increase Patient Knowledge and Promote Understanding

- Diabetes, cardiorenal, and metabolic diseases as chronic conditions
  - Types of diabetes, lipid disorders, etc
  - Microvascular and macrovascular complications
- What exams and tests to expect for eyes, kidney, feet, heart, hearing
- "Know and understand your numbers": BMI, A1C, TIR, FPG, BP, LDL-C, TG, HDL-C, non-HDL-C, eGFR, UACR
- Treatment options: lifestyle, pharmacologic, surgical/invasive interventions
- Healthcare systems and reimbursement

Motivational Interviewing

- Ask open-ended questions
- Affirm personal challenges and goals
- Encourage belief patient can control health outcomes (ie, self-efficacy)
- Summarize discussions

Tailor to Individual Patient

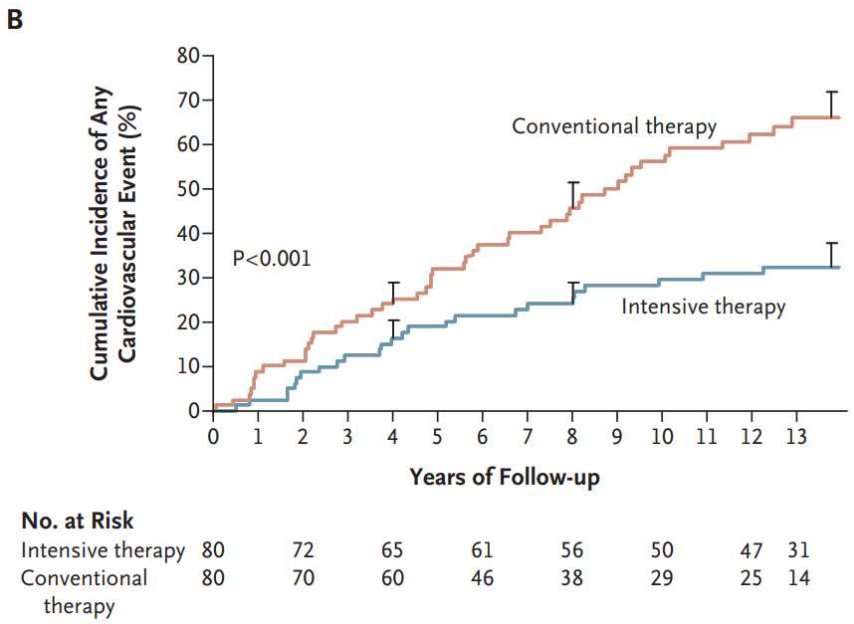
- Health literacy
- Socioeconomic considerations and other social determinants of health

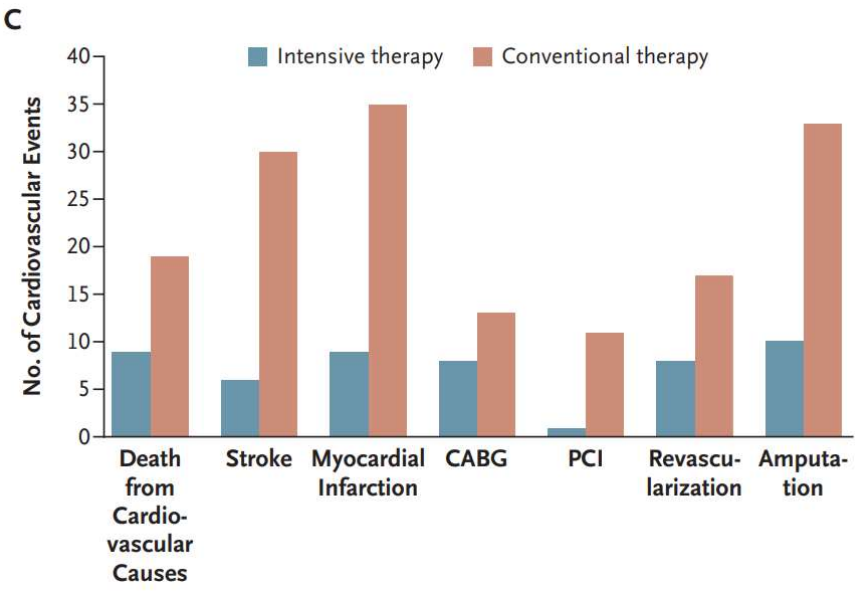
Improve Adherence

A1C = hemoglobin A1C, BMI = body mass index; BP = blood pressure; eGFR = estimated glomerular filtration rate; FPG = fasting plasma glucose; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TG = triglycerides; TIR = time in range; UACR = urine albumin-creatinine ratio.

STENO-2 Trial: Multipronged Approach to CV Risk Reduction

In at-risk patients with T2DM, an intensive intervention with multiple drug combinations and behavior modification had sustained beneficial effects with respect to vascular complications and on rates of death from any cause and from CV causes





CABG = coronary-artery bypass grafting; HR = hazard ratio; PCI = percutaneous coronary intervention.

Gæde P, et al. *N Engl J Med.* 2008;358(6):580-591.

Management of Lipids in Diabetes, Cardiorenal, and Metabolic Diseases

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

Monitor Lipids Every 6-12 Weeks Until Individual Target Is Achieved

LDL-C Goal—Reduce LDL-C by ≥50% or Reach Risk-Based Goal, Whichever Is Lower

<100	**High**	≥2 RF + 10-y risk 10-20% ***or*** diabetes or CKD ≥3, no other RF
<70	**Very high**	ASCVD, ACS, PAD, or 10-y risk >20% Diabetes + ≥1 RF CKD ≥3 with albuminuria HeFH
<55	**Extreme**	Progressive ASCVD despite LDL-C <70 mg/dL ASCVD + diabetes or CKD ≥3 or HeFH Premature ASCVD (<55 years, male; <65 years, female)
<40 mg/dL	**Extreme-plus**	Extreme risk plus second event in 2 years

Expected Decrease in LDL-C

Statin	PCSK9i	Eze	Eze + BA	BA	BAS
↓ ~30-60%	↓ ~60%	↓ ~20%	↓ ~38%	↓ ~20%	↓ ~20%

- Initial combination therapy when LDL-C is >50% higher than goal
- Add treatments every 6-12 weeks until goal is achieved

Management of Hypertriglyceridemia

Reduce risk of ASCVD	
All patients with elevated TG	Low-fat, moderate-CHO diet and other lifestyle + max-tolerated statin
Patients with TG 135-499 mg/dL + ASCVD or diabetes + 2 RF	Add IPE
Others with TG <500 mg/dL	Consider adding fibrate, OM3,[a] or niacin
Reduce risk of pancreatitis	
All patients with TG >500 mg/dL	Low-fat, moderate-CHO diet and other lifestyle + max-tolerated statin Add fibrate, OM3,[a] or niacin
Patients with insulin resistance	Consider adding pioglitazone
Patients with acute, severe hypertriglyceridemia	Consider insulin

Expected Decrease in TG

Statin	Fibrate	OM3[a]	Niacin	Pio
↓ ~20-30%	↓ ~30-50%	↓ ~30-40%	↓ ~20-30%	↓ ~10-15%

Proven ASCVD benefits in CVOTs

[a] IPE, EPA, or EPA+DHA.

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; BA = bempedoic acid; BAS = bile acid sequestrant; CKD ≥3 = stage 3 chronic kidney disease; CVOT = cardiovascular outcome trial; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; Eze = ezetimibe; HDL-C = high-density lipoprotein cholesterol; HeFH = heterozygous familial hypercholesterolemia; IPE = icosapent ethyl; LDL-C = low-density lipoprotein cholesterol; OM3 = prescription-strength omega-3 fatty acid; PAD = peripheral artery disease; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; Pio = pioglitazone; RF = major risk factors (ie, advancing age, elevated non-HDL-C, elevated LDL-C, low HDL-C, diabetes, hypertension, CKD, cigarette smoking, family history of ASCVD); TG = triglyceride.

Management of Lipids in Diabetes, Cardiorenal, and Metabolic Diseases

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

Goal BP[a]: <130/80 mm Hg

Assess BP at Home Weekly and in Office Every 3-12 Months[b]	
Seated BP	Back supported, feet flat on ground with oscillometric device connected; let patient rest quietly for 2 minutes before checking BP twice, 1 min apart, followed by 1 orthostatic reading
Orthostatic BP[c]	Assess standing BP for evaluation of volume depletion and autonomic dysfunction[d]
Ambulatory BP	Train patient how to measure seated BP at home upon waking. Transmit BP data via Bluetooth or via fax to patient chart

Preferred BP-lowering Agents	Treatment Regimen
1. ARB or ACEi at maximum tolerated dose[e]	• Use initial combination therapy if BP >20/10 mm Hg above goal • Add medications as needed to reach goal • Use combination products to foster adherence
2. Dihydropyridine CCB	
3. Thiazide-type diuretic	
4. Spironolactone for resistant hypertension[f]	

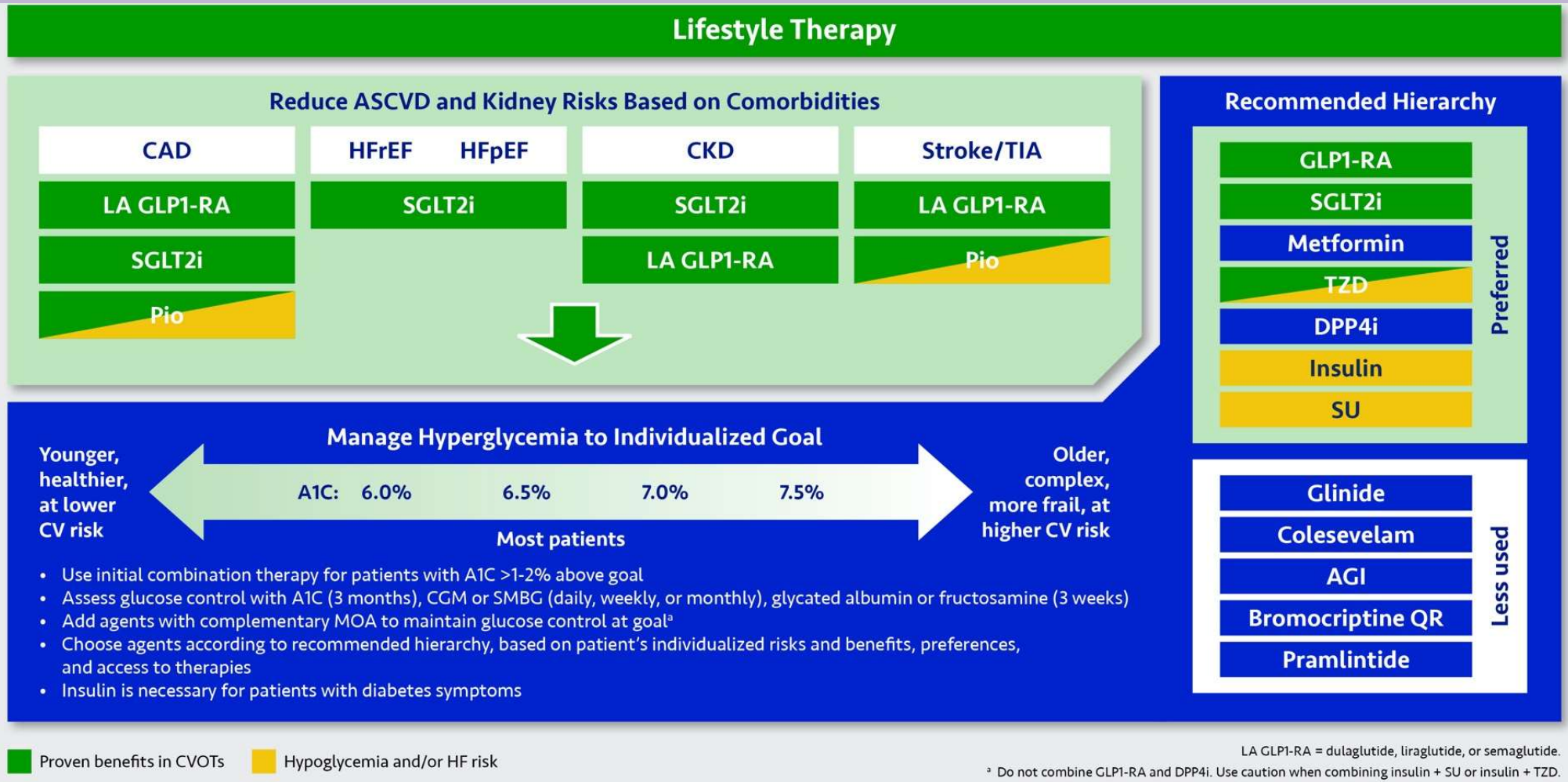
[a] Individualize based on patient characteristics. Maintain DBP >60 mm Hg in older adults with diabetes. [b] Check BP more frequently when starting or titrating therapy. [c] BP decrease of ≥20/10 mm Hg within 3 minutes of standing.
[d] Indicates higher risk of cardiovascular events and mortality. [e] Preferred for kidney and cardiovascular protection. [f] Other MRAs (i.e., finerenone and eplerenone) not shown to significantly reduce BP.

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BP = blood pressure; CCB = calcium channel blocker; DBP = diastolic blood pressure; MRA = mineralocorticoid receptor antagonist.

Antihyperglycemic Therapy

Prevent CVD/CKD Events Regardless of Glycemic Status
Manage Glycemia to Individualized, Established Goals

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.

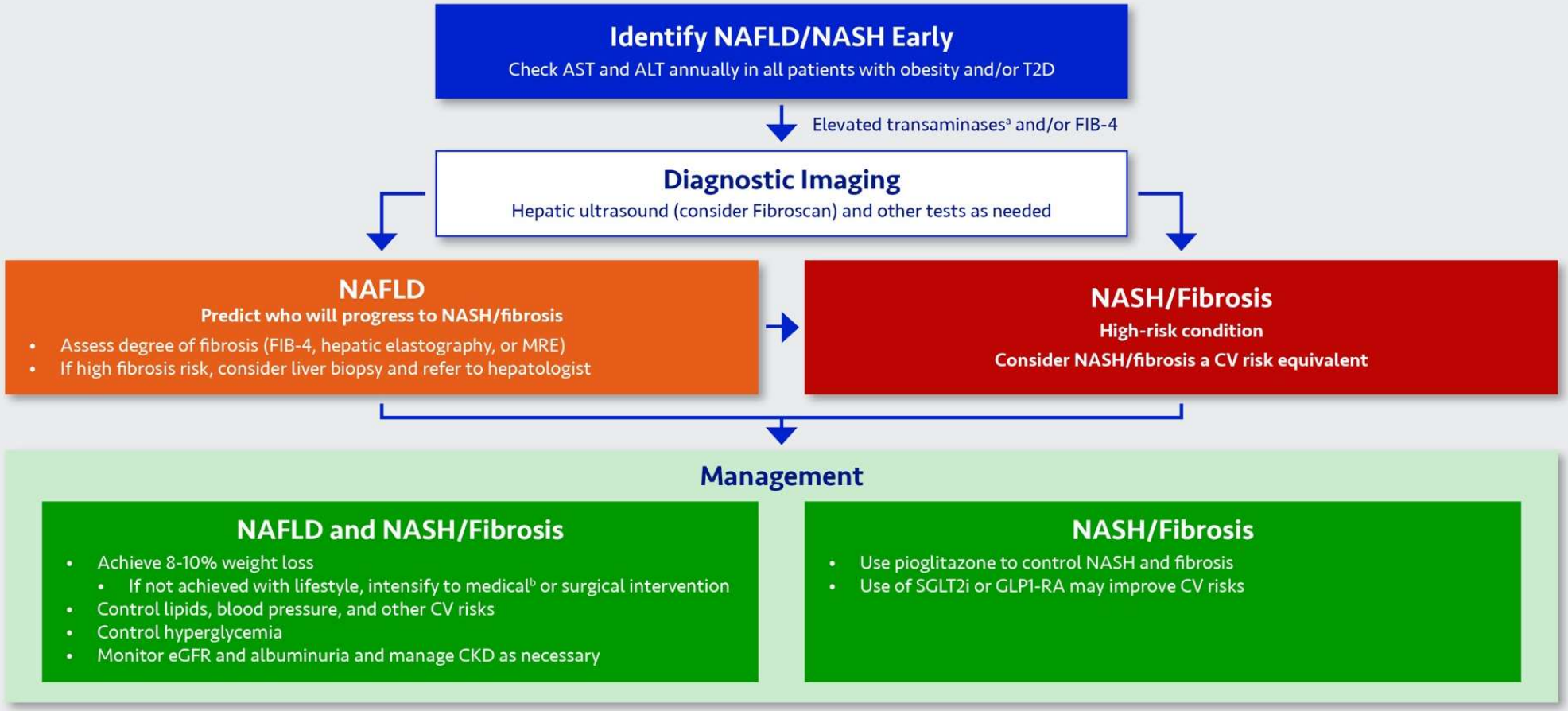


LA GLP1-RA = dulaglutide, liraglutide, or semaglutide.

[a] Do not combine GLP1-RA and DPP4i. Use caution when combining insulin + SU or insulin + TZD.

Management of NAFLD and NASH

Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.



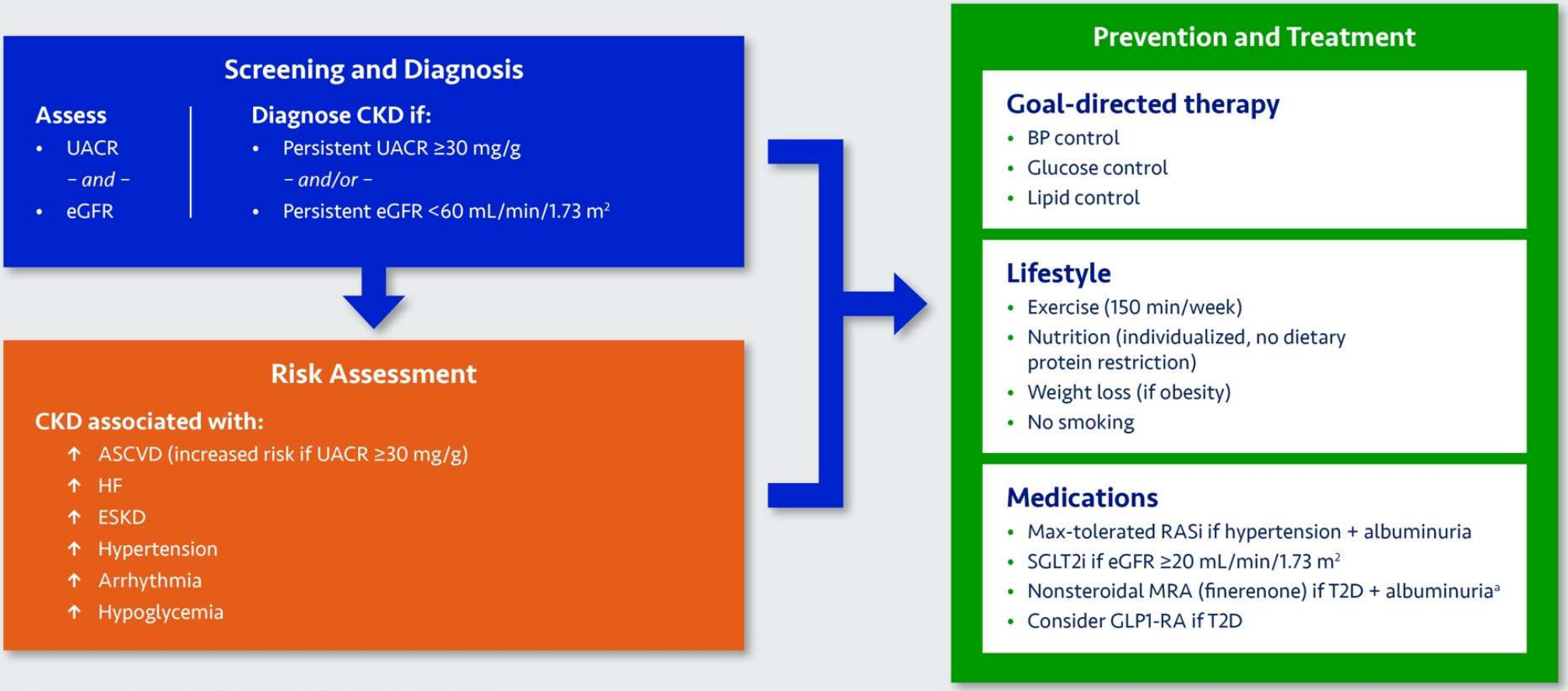
[a] Fatty liver disease can develop even if LFTs are normal, especially in individuals with insulin resistance.

[b] Semaglutide, liraglutide, orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion.

ALT = alanine transaminase; AST = aspartate transaminase; CV = cardiovascular; FIB-4 = fibrosis 4 calculation; GLP1-RA = glucagon-like peptide 1 receptor agonist; LFT = liver function test; MRE = magnetic resonance elastography; NAFLD = nonalcoholic fatty liver disease; NASH = nonalcoholic steatohepatitis; SGLT2i = sodium glucose cotransporter 2 inhibitor; T2D = type 2 diabetes.

CKD Diagnosis and Treatment

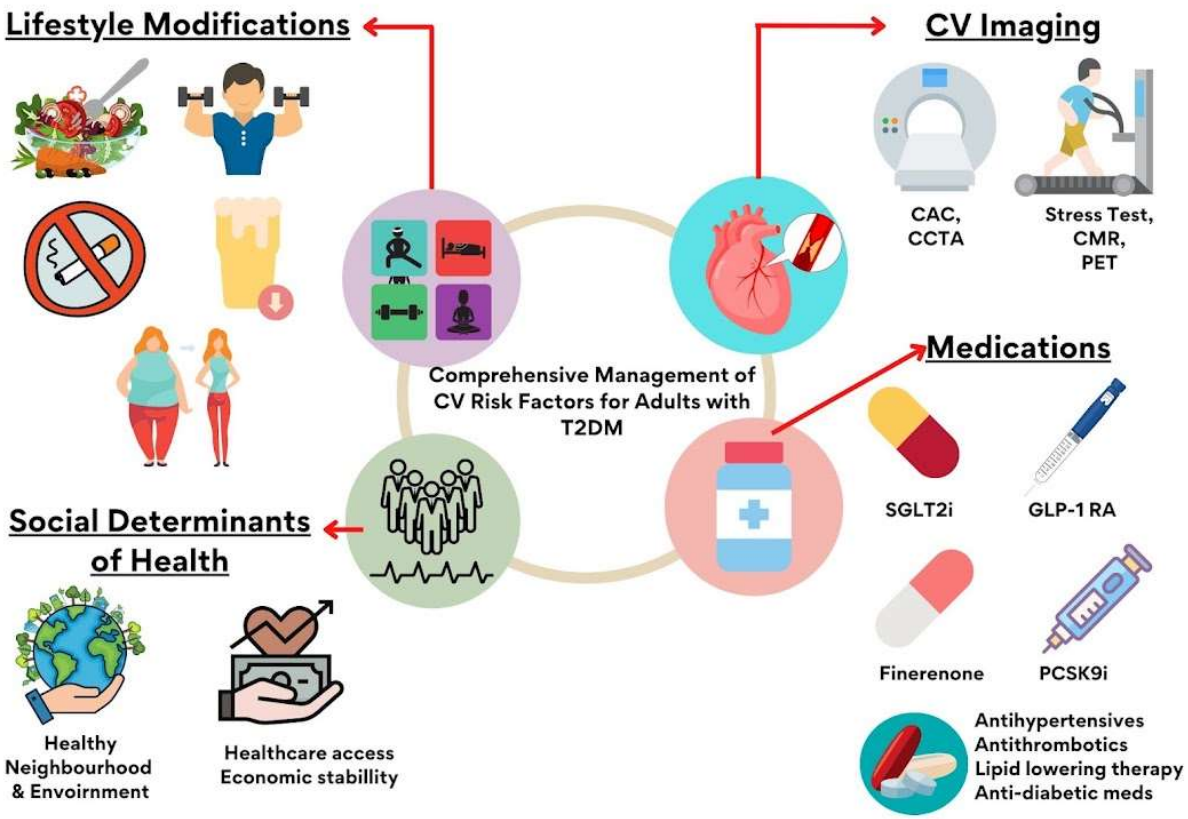
Handelsman Y...**Michos ED**... et al. DCRM Multispecialty Practice Recommendations. J Diabetes Complications. 2022;36(2):108101.



[a] Outcomes evidence only available for finerenone. Albuminuria = UACR ≥30 mg/g.

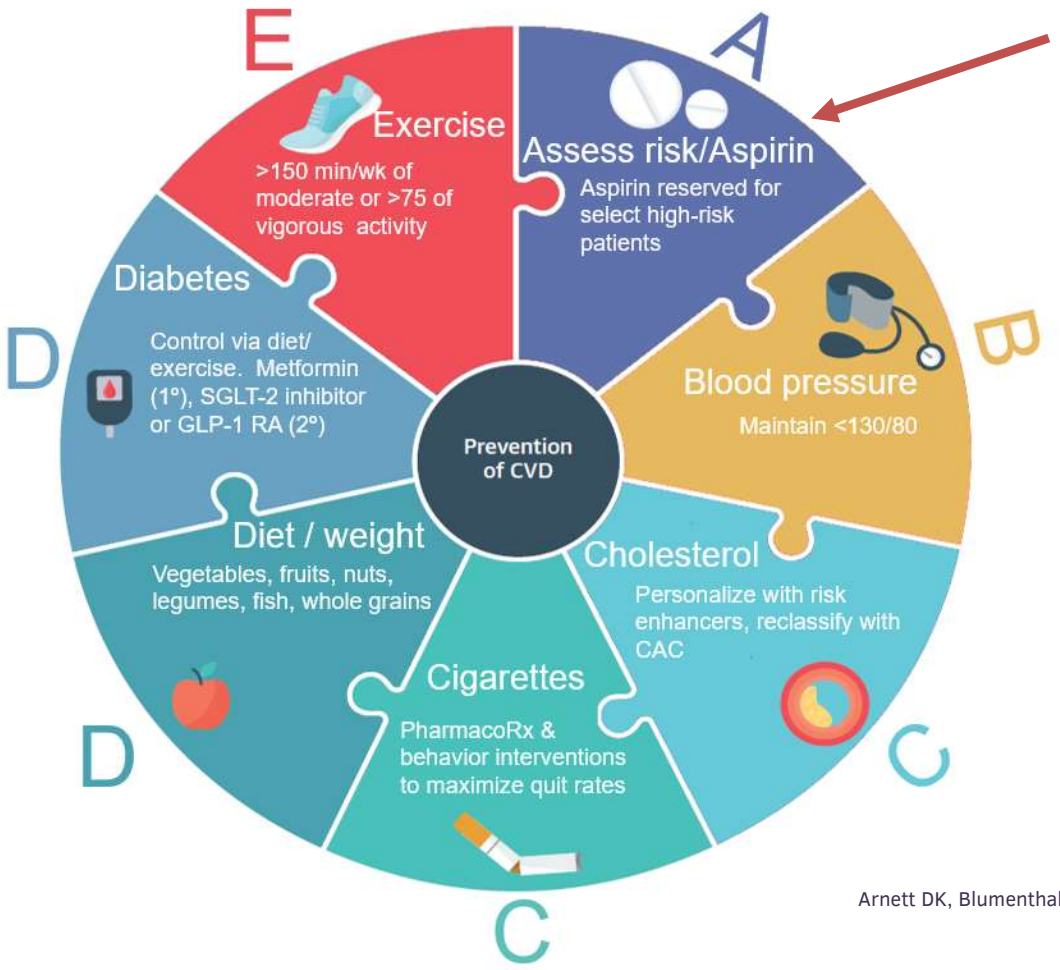
ASCVD = atherosclerotic cardiovascular disease; BP= blood pressure; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP1-RA = glucagon like peptide 1 receptor agonist; HF = heart failure; MRA = mineralcorticoid receptor agonist; RASi = renin angiotensin system inhibitor; SGLT2i = sodium glucose cotransporter 2 inhibitor; T2D = type 2 diabetes; UACR = urine albumin-creatinine ratio.

2022 AHA Statement on Comprehensive Management of CV Risk Factors For Adults with T2D



Jha K., Adhikari R, Blumenthal R, Blaha M- ACC Expert Analysis 2022

To lower CVD Risk, Follow ABCDE's of Prevention



Arnett DK, Blumenthal RS,....**Michos ED**...et al. Circulation 2019

Conclusions

- Obesity, Prediabetes, Diabetes, and Metabolic Syndrome overlap and are highly prevalent
- Weight loss through lifestyle (and pharmacotherapy as needed) can simultaneously improve multiple CV risk factors (BP, lipids, A1c) and reduce risk of downstream CVD (HF, Afib, ASCVD).
- Time is ticking – longer duration of exposures to cardiometabolic risk factors confers greater CVD risk
- Early diagnosis and implementation of preventive strategies is key.
- Assessment of CV risk guides intensity of treatment
- Social determinants of health bring challenges to our patients – assess & address
- Language matters. Use patient first language – person before their diagnosis.
- A team-based multidisciplinary approach is needed, with the patient at the center

Cardiometabolic teleECHO™ Clinic

Patient Recommendation Form

Presentation Date: Nov 2, 2022, **Presenter name:** **Brenda Grant, MD**

64 y/o male with uncontrolled diabetes complicated by retinopathy, proteinuria (>300mg/dl), peripheral neuropathy, dyslipidemia, HTN, Afib and ASCAD, sleep apnea and BMI 45 (135kg). A1C 9.1% on MDI and possible financial issues.

Levemir	55 units	BID
Novolog	25 units	TID
metformin	1000mg	BID
sitagliptin	100mg	daily
pioglitazone	30mg	daily
atorvastatin	40mg	daily
metoprolol succinate	25mg	daily
isosorbide mononitrate	15mg	daily
Eliquis	5mg	BID
gabapentin	400mg	TID PRN
Amitriptyline	100mg	Bedtime PRN

Case Recommendations:

In general, in our experience we have managed patients who have similar problems with the approach of:

1. Small changes for nutrition and consider targeting breakfast and 4th meals and as you discussed with him limiting fried food and chips.
2. Continue to explore ideas for activity such as biking as he suggested to increase steps.
3. Encourage regular use of CPAP.
4. Consider duloxetine as an aid for both neuropathic pain and depression to goal 120 mg. Additionally consider discussing possible counseling and support group for whole body health.
5. Attempt to decrease amitriptyline as may be contributing to craving and weight gain first 50mg then trial off as increase duloxetine.
6. Limit or stop gabapentin as able.
7. Consider referral for bariatric surgery.

8. Use of 340B formulary to start liraglutide 0.6 units and increase every 7-10 days if tolerating it well, if his Medicare does not cover weekly GLP-1 RA affordably.
9. Attempt to get weekly semaglutide through PAP or use it initially if not significant cost to patient 0.25mg weekly for 2-3 weeks then then 0.5mg with goal over 3 months to 2mg dose if able.
10. Review injection site for lipodystrophy.
11. Reduce Levemir to 68 units in the morning- once a day from 55 bid and if am running less than 100 for more than 2 days in a row or any less thank 70mg/dl reduce by 4 units.
12. Continue prandial insulin at 25units unit three times a day- but low threshold to reduce by 3 for lower blood sugars as increase GLP- 1 RA.
13. Stop sitagliptin.
14. Convert metformin to 2 tablets 750mg Daily from 1000mg bid.
15. Add lisinopril in 1-2 months for blood pressure and for proteinuria.
16. Consider addition of dapagliflozin or empagliflozin in 2-3 months so not to overwhelm pt. initially.
17. Consider u500 insulin in the future if sugars still uncontrolled on GLP-1 RA
18. Consider increase atorvastatin to 80mg.
19. Reassess triglycerides in 6-12 months.

Nicole Ehrhardt, MD

Physician Signature: *Nicole Ehrhardt*
Please Re-present case: Dec 2022