Prevention and management of patients with cardio-renal-metabolic comorbidities

Jennifer Crowley, PharmD, BCPS, BCCP

August 22, 2024

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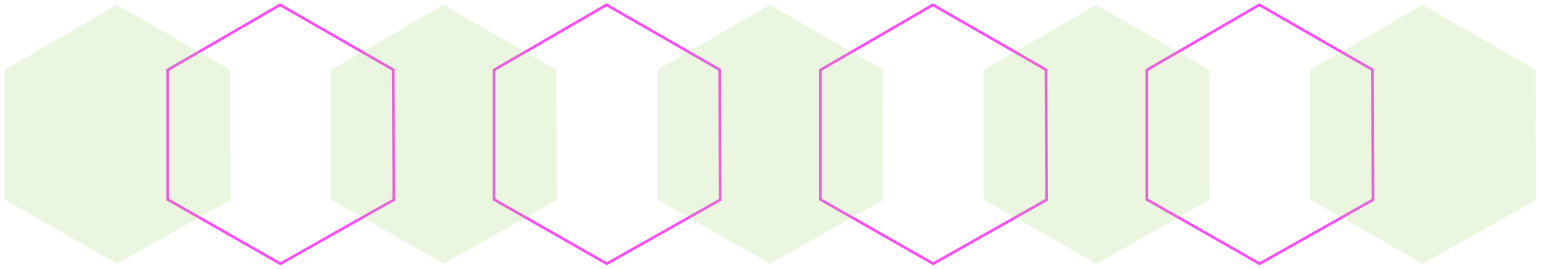
SOMOS MÁS FUERTES

CONVENCIÓN ANUAL
CFPR 2024

Disclosure to Learners



Jennifer Crowley, faculty for this CE activity, has no relevant financial relationship(s) with ineligible companies to disclose.

“The Colegio de Farmacéuticos de Puerto Rico is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.”

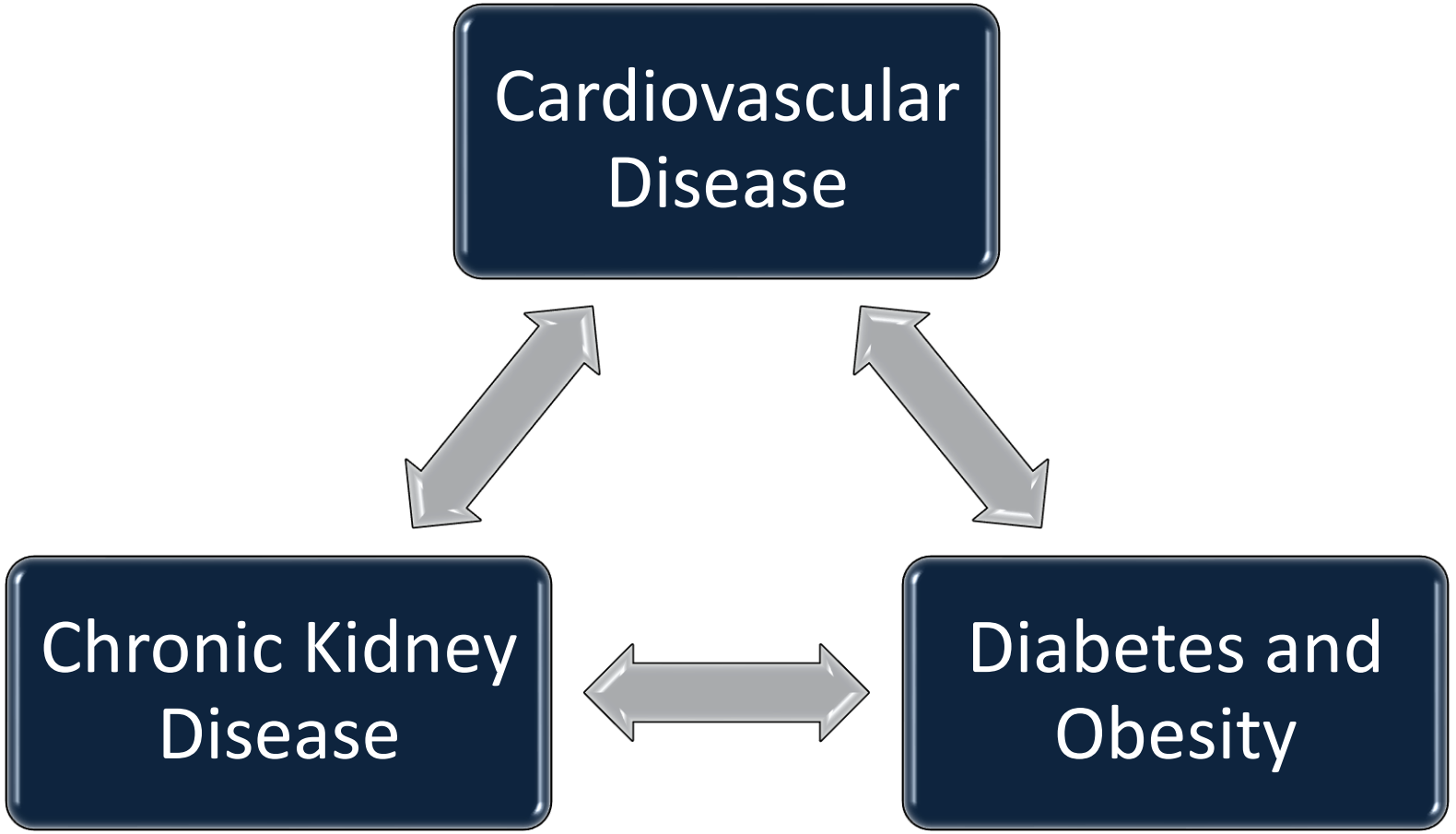
Provider Number: 0151

Objectives

1. Discuss the pathophysiologic relations between metabolic conditions, cardio, and renal associated diseases
2. Identify risk reduction strategies to prevent cardio-renal-metabolic comorbidities
3. Discuss evidence-based data that support the use of medications to prevent cardio-renal-metabolic comorbidities
4. Describe place in therapy of the different pharmacologic interventions to prevent and manage metabolic-cardio-renal comorbidities
5. Analyze the differences in incretin-based, sodium-glucose cotransporter 2 inhibitors and other therapies related to cardiorenal protection
6. Explain risks and benefits of medications in people with diabetes, heart failure, and/or chronic kidney disease to prevent or manage comorbidities
7. Value the role of the pharmacist as a member of the interprofessional team caring for these patients

Pre-Test

1. Guidelines are shifting from treatment of diabetes as the only condition to reduction of overall cardio-renal-metabolic comorbidities. True or False
2. To reduce overall mortality in patients with T2D, sitagliptin is preferred in those with HF or CKD. True or False
3. In patients with high risk of ASCVD or with established CVD, GLP-1RAs and SGLT2is are preferred agents. True or False
4. Clinical pharmacists can help identify patients with diabetes who may benefit from GLP-1 RAs or SGLT2is to optimize their glycemic control and provide positive cardiorenal benefits. True or False
5. Pharmacists can educate team members on the benefits and risks of SGLT2 inhibitors or GLP-1RA beyond glycemic control. True or False


Cardiovascular Disease
Chronic Kidney Disease
Diabetes and Obesity

A word on vernacular…

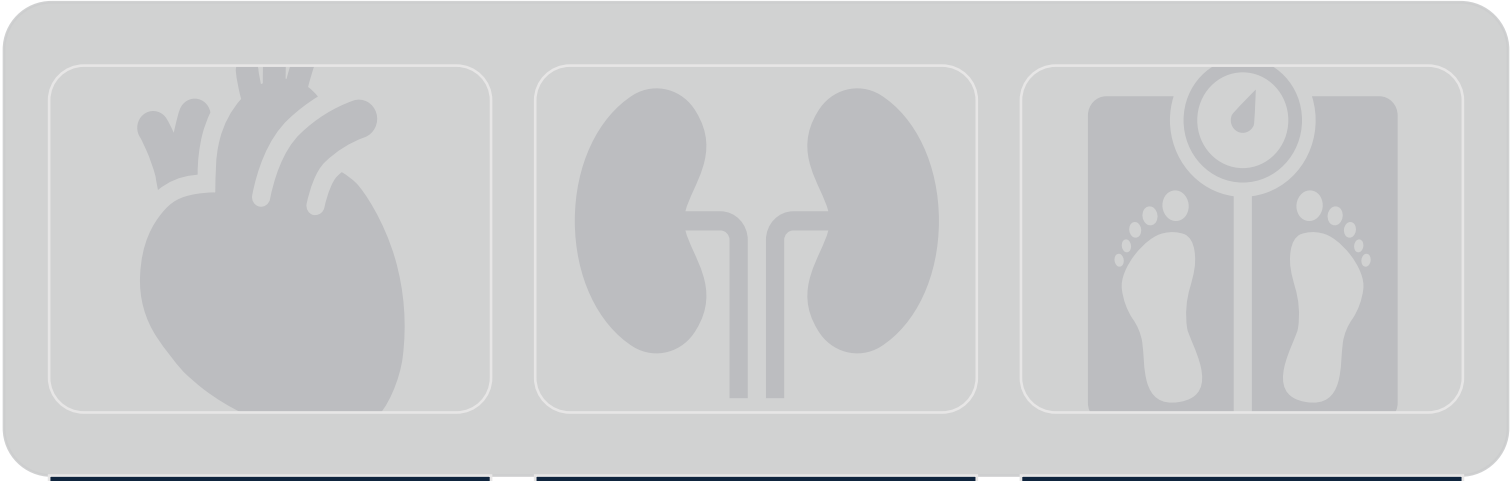
Avoid

- Defining patients by a disease
- “Obese…diabetic…renal patients”
- Negative/judgmental terms
- “Heavy,” “fat,” or “weight problem”

Use

- Person-first language
- “People with….obesity…diabetes…”
- Positive language
- Ask permission, stay curious

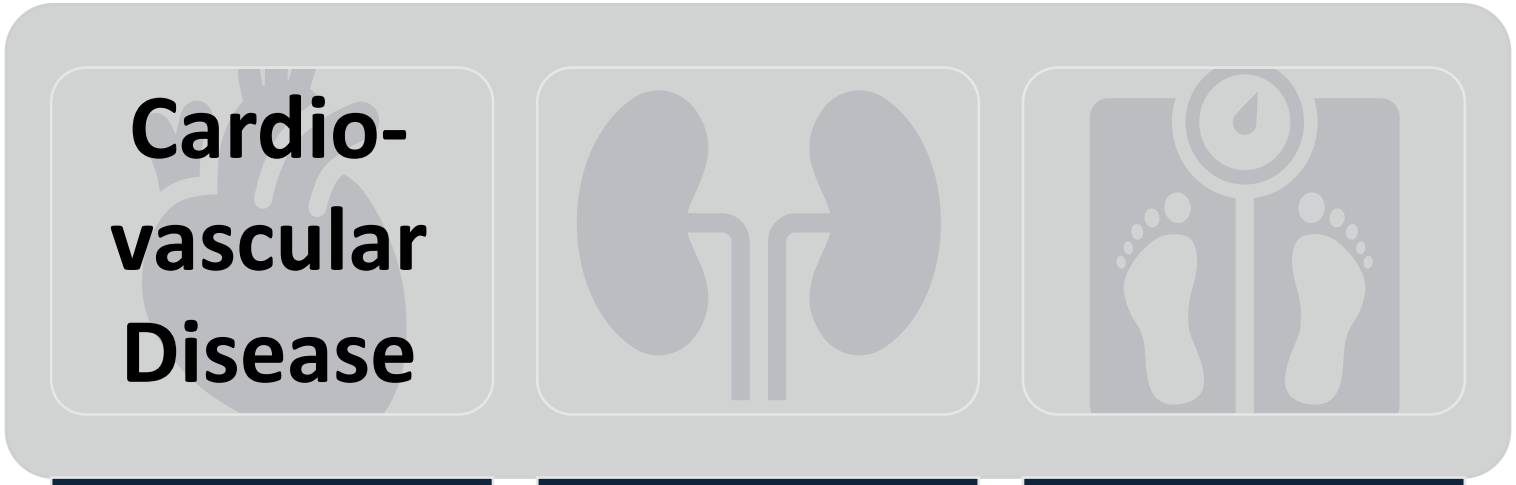
American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.
National Institute of Diabetes and Digestive and Kidney Diseases. Health Information for Health Professionals: Talking with your patients about weight. August 2023. Accessed July 28, 2024.



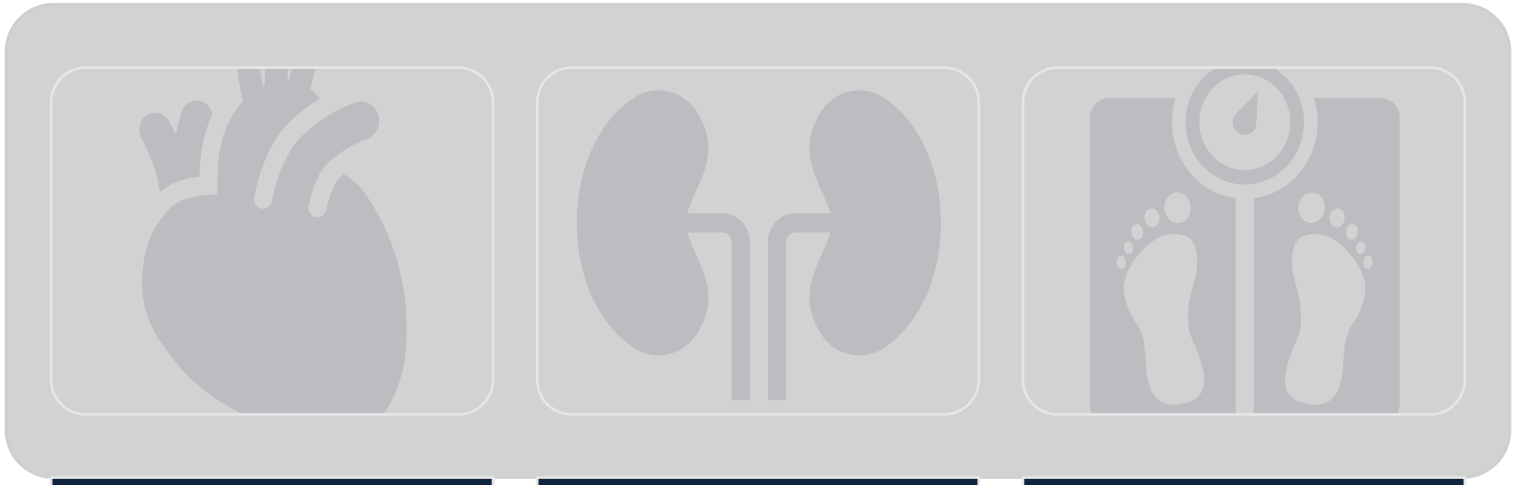
Cardio-vascular Disease

Chronic Kidney Disease

Diabetes and Obesity



Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

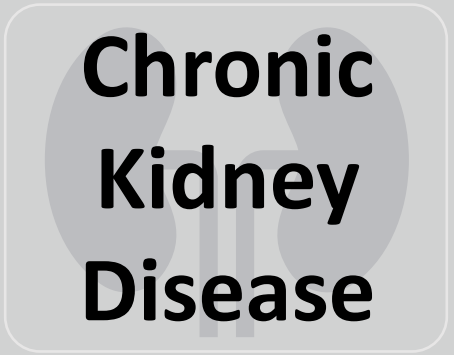


Cardio-vascular Disease

Chronic Kidney Disease

Diabetes and Obesity

Chronic Kidney Disease

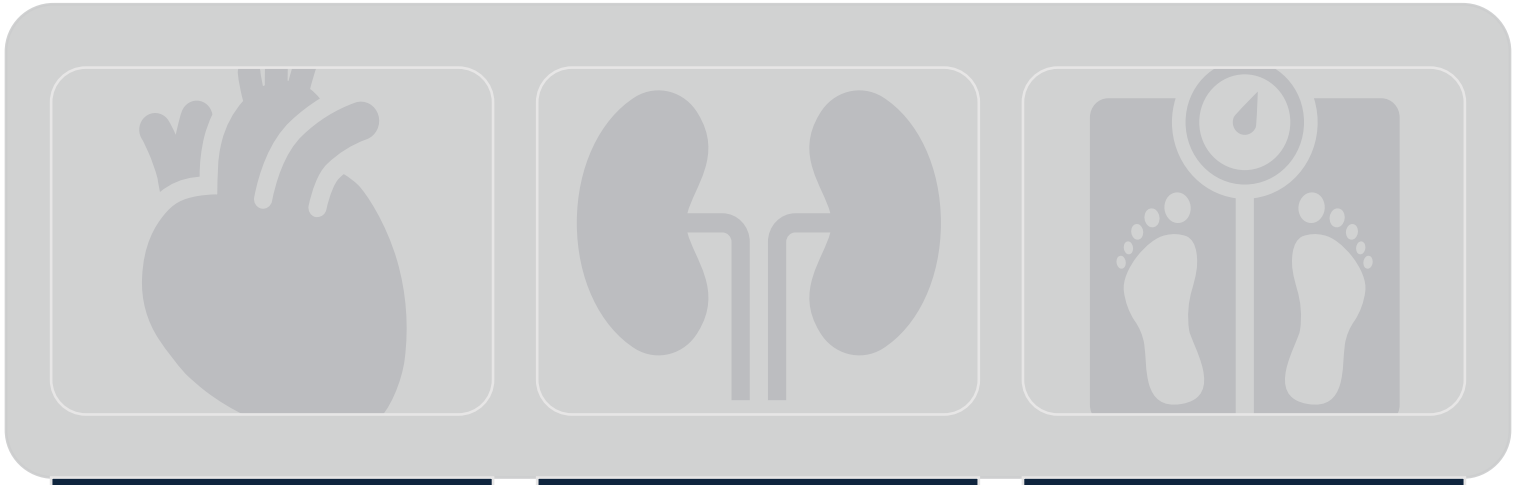


Cardio-vascular Disease

Abnormality of kidney structure or function present for ≥ 3 months

Diabetes and Obesity

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314.



Cardio-vascular Disease

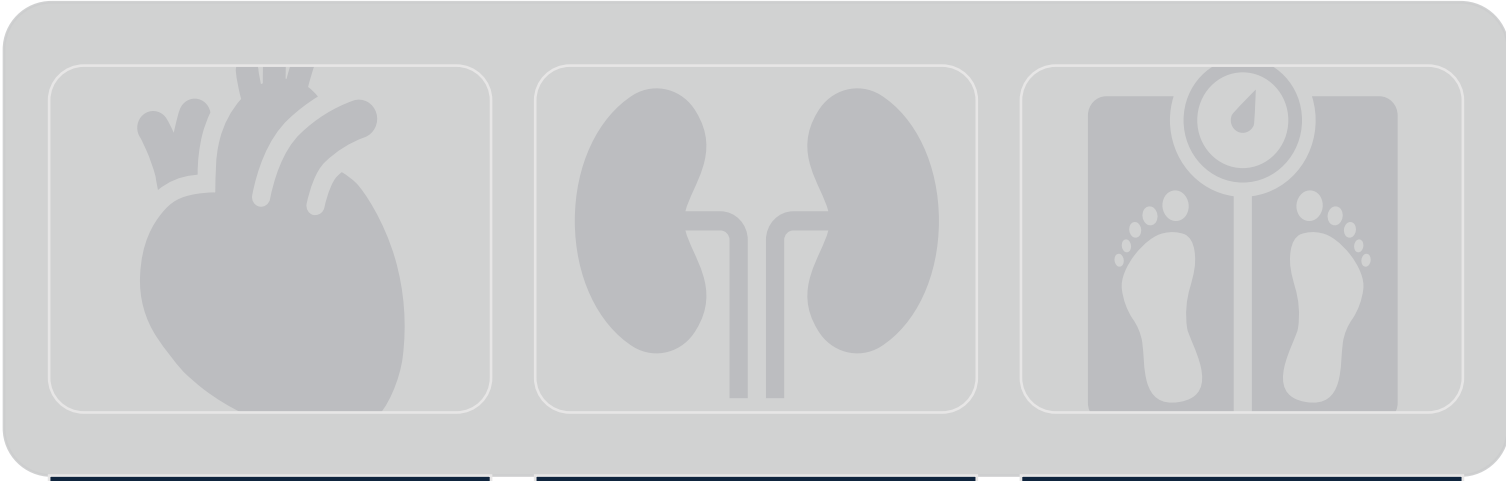
Chronic Kidney Disease

Diabetes and Obesity

Diabetes and Obesity

Cardio-vascular Disease	Chronic Kidney Disease	A1C ≥ 6.5% FBG ≥ 126mg/dL 2HPPG ≥ 200mg/dL Sxs w/ random BG ≥ 200mg/dL --- BMI ≥ 30 kg/m^2

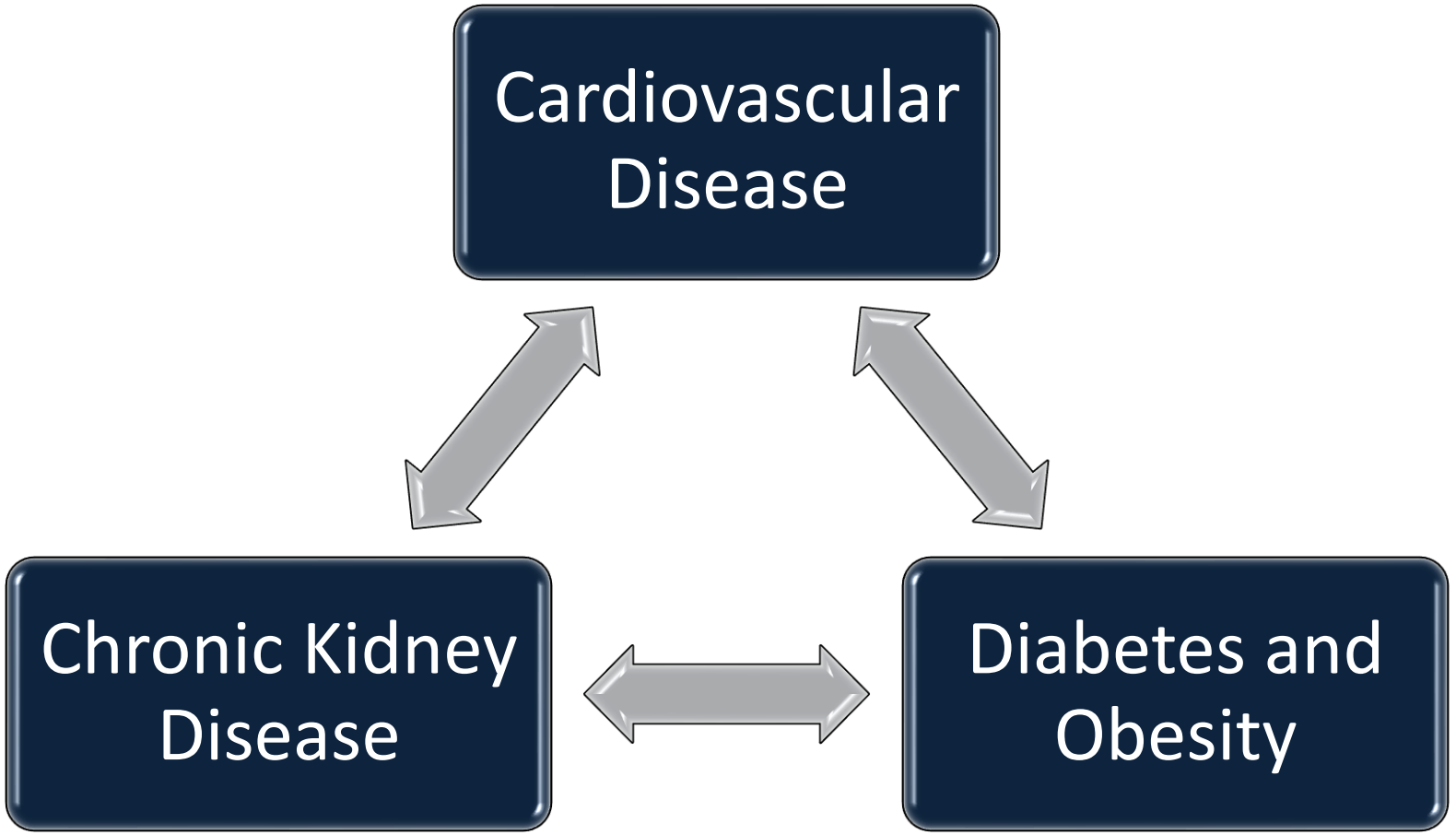
American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.
World Health Organization. Fact sheets: obesity and overweight. 1 March 2024. Accessed July 26, 2024.



Cardio-vascular Disease

Chronic Kidney Disease

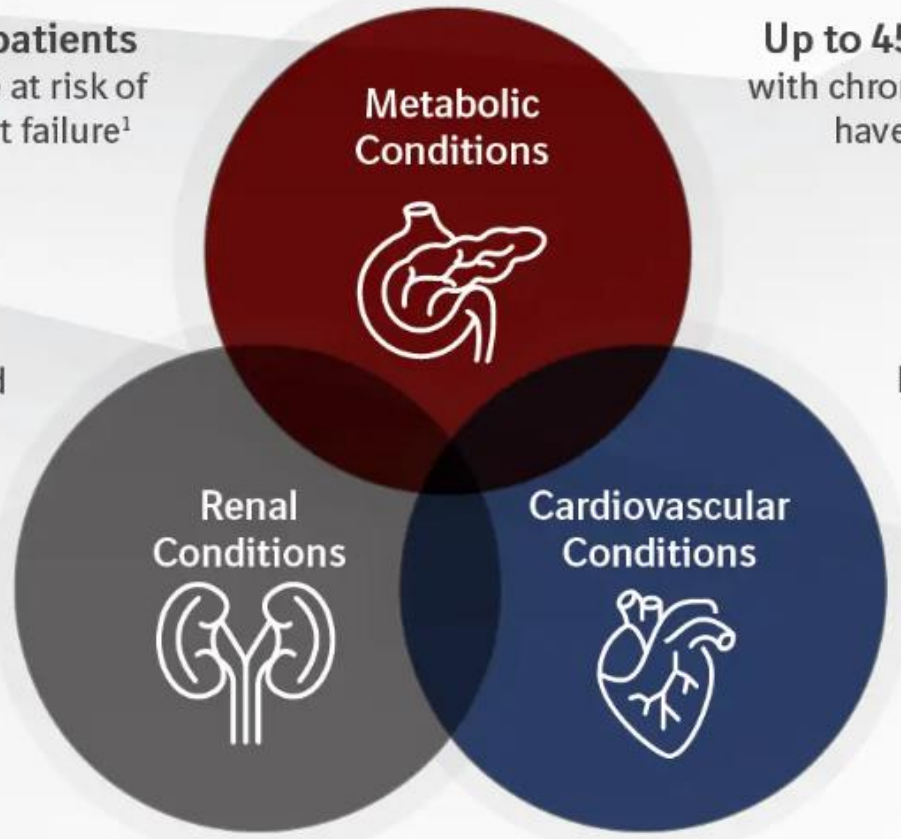
Diabetes and Obesity


Cardiovascular Disease
Chronic Kidney Disease
Diabetes and Obesity

Shared Risk Factors Compound the Impact of Cardio-Renal-Metabolic Conditions

Up to 50% of patients with diabetes are at risk of developing heart failure[1]

Up to 45% of people with chronic heart failure have diabetes[7]



36.5% of adults with diabetes have been diagnosed with chronic kidney disease[2]

Rate of hospitalization for heart failure **>4x greater** in patients with diabetes[6]

Chronic kidney disease prevalence is **3x higher** in patients with diabetes[2]

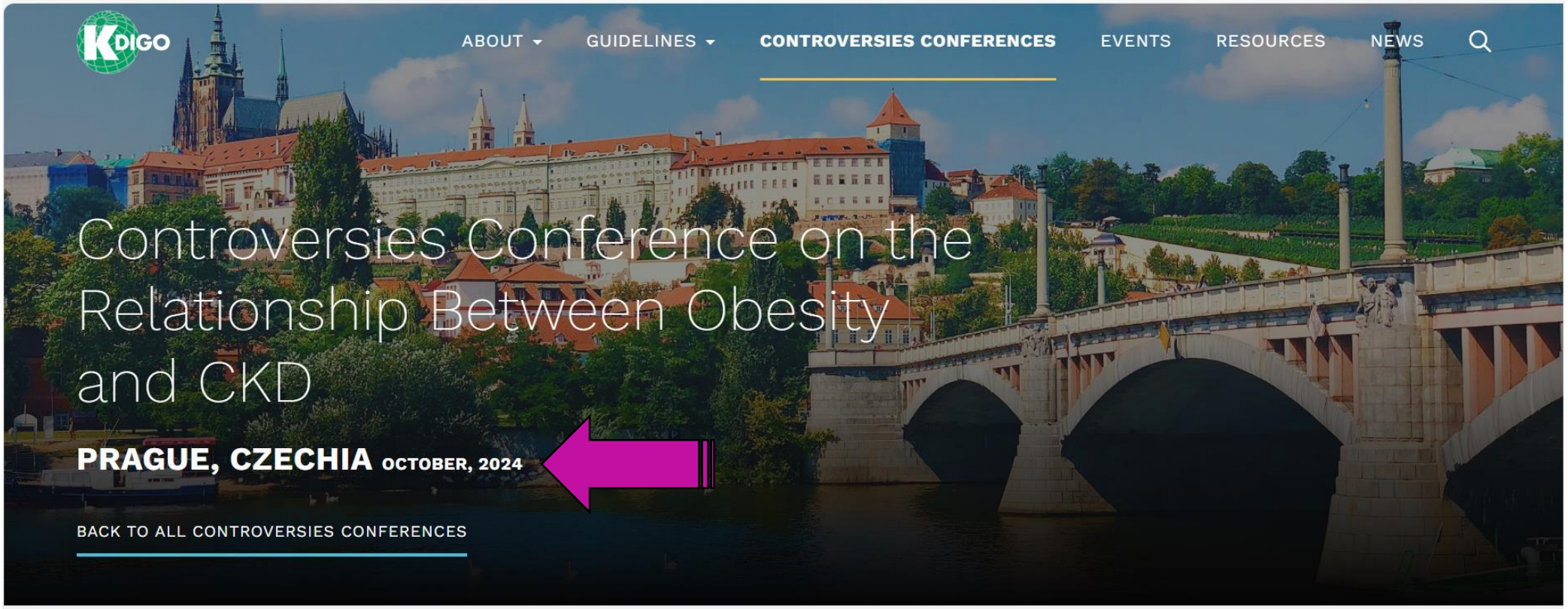
CV disease causes **2 out of 3 deaths** in people with diabetes[5]

63% of patients with chronic kidney disease have CV disease, compared to 5.8% of adults without[4]

Over 60% of heart failure patients have kidney disease[4]

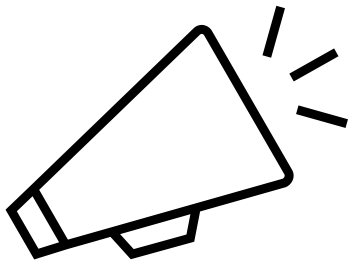
Wright E. Understanding the interconnectivity of the cardiovascular, renal and metabolic systems. 2023. https://www.cardio-renal-metabolic.com

New news?...



Kidney Disease: Improving Global Outcomes (KDIGO) . Conferences – KDIGO. https://kdigo.org/conferences/

…Or old news?



ELSEVIER

Journal of the American College of Cardiology

Volume 57, Issue 23, 7 June 2011,

State-of-the-Art Paper

Triad of Metabolic Syndrome, Chronic Kidney Disease, and Coronary Heart Disease With a Focus on Microalbuminuria: Death by Overeating

Freij Gobal MD *, Abhishek Deshmukh MD *, Sudhir Shah MD †, Jawahar L. Mehta MD, PhD *

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https://doi.org/10.1016/j.jacc.2011.02.027

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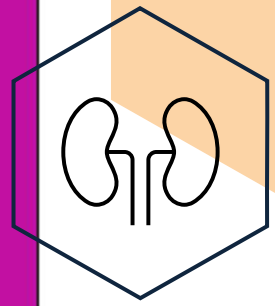
Freij Gobal, A. et al. Triad of Metabolic Syndrome, Chronic Kidney Disease, and Coronary Heart Disease With a Focus on Microalbuminuria: Death by Overeating. Journal of the American College of Cardiology, Volume 57, Issue 23, 2011, Pages 2303-2308.



Cardiovascular-Kidney-Metabolic (CKM) Syndrome

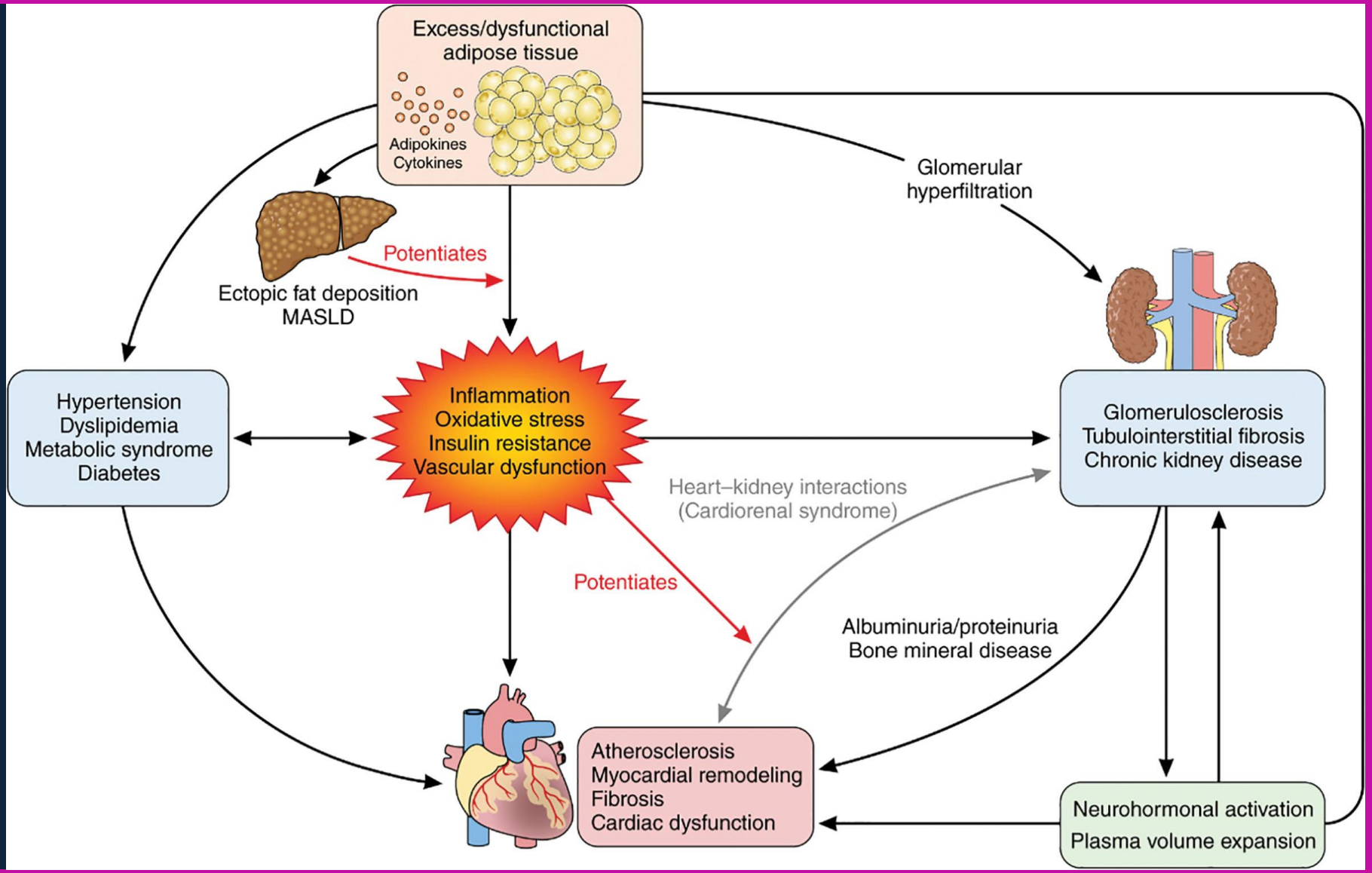
Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

AHA Definition

"CKM syndrome is a systemic disorder characterized by pathophysiological interactions among metabolic risk factors, CKD, and the cardiovascular system leading to multiorgan dysfunction and a high rate of adverse cardiovascular outcomes. CKM syndrome includes both individuals at risk for CVD due to the presence of metabolic risk factors, CKD, or both and individuals with existing CVD that is potentially related to or complicates metabolic risk factors or CKD. The increased likelihood of CKM syndrome and its adverse outcomes is further influenced by unfavorable conditions for lifestyle and self-care resulting from policies, economics and the environment."

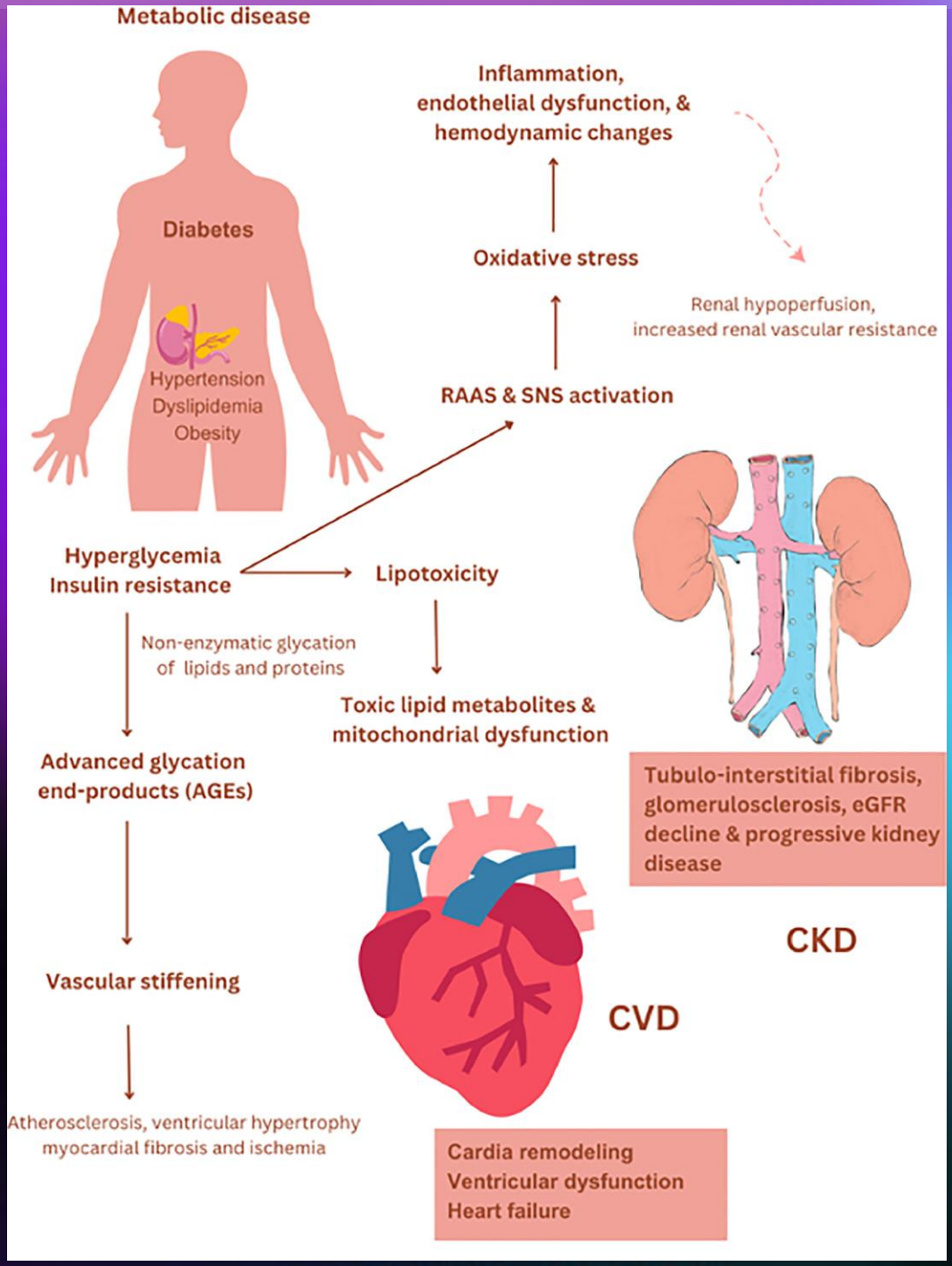
Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

Pathophysiology



Ndumele CE, Neeland IJ, Tuttle KR, et al. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(20):1636-1664.

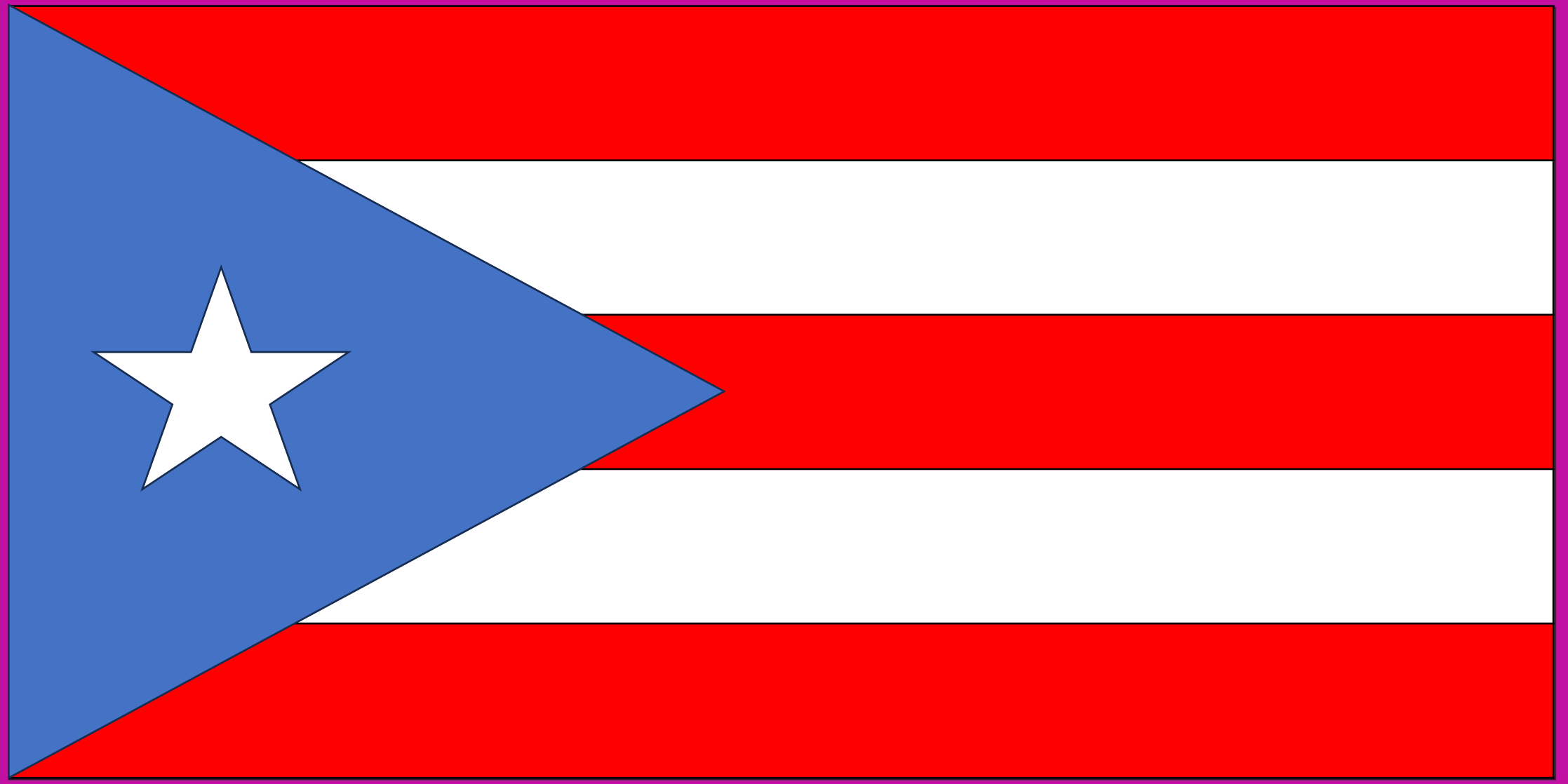
- ***Begins with***: excessive and dysfunctional adipose tissue
- ***Leads to***: hypertension, hypertriglyceridemia, MetS, CKD, and type 2 DM
- ***Ends in***: coronary artery calcifications, decrease in kidney function, increase in mortality



Sebastian SA, Padda I, Johal G. Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review. *Current Problems in Cardiology*, Volume 49, Issue 2, Feb 2024.

Patient Awareness

- How are CKD, CVD, and Diabetes Related? | The Kidney Disease, Heart Disease, and Diabetes Connection (youtube.com)



Behavioral Risk Factor Surveillance System

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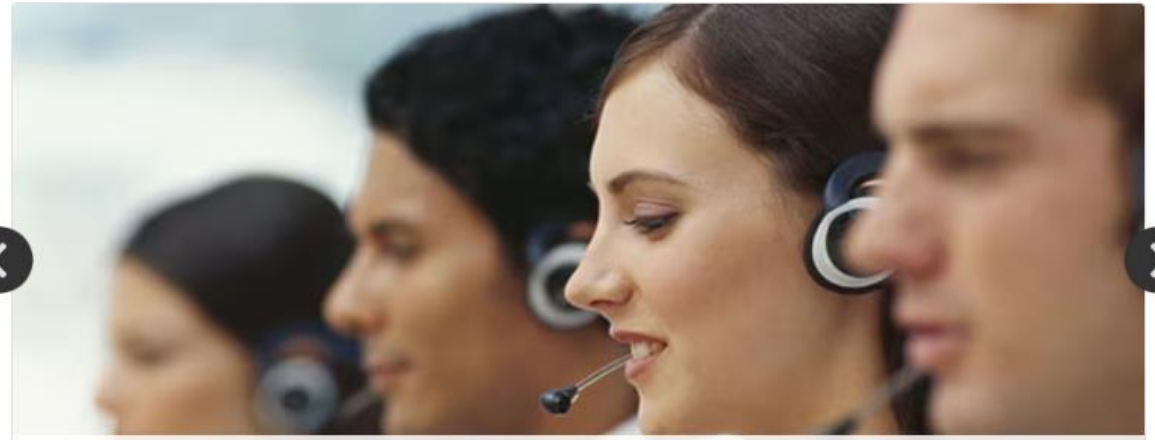


2022 BRFSS Data Now Available

View the latest 2022 BRFSS Annual Data

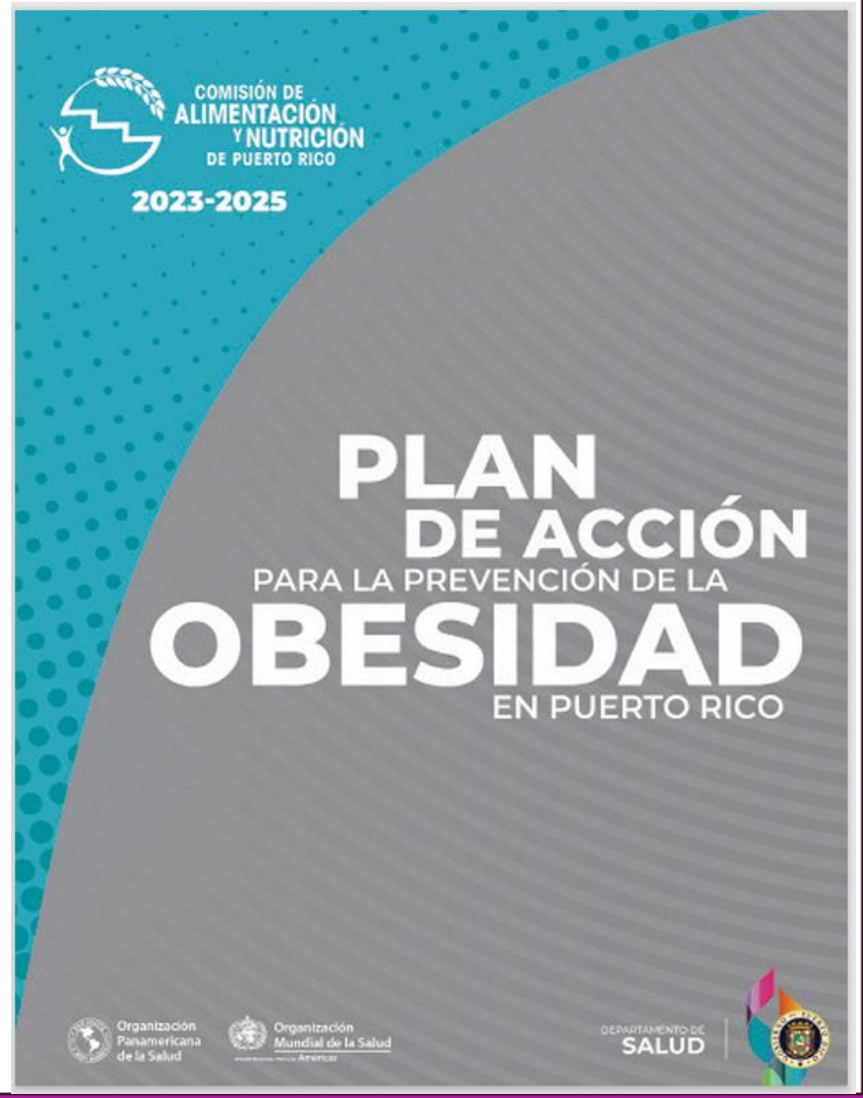
BRFSS™

The Behavioral Risk Factor Surveillance System (BRFSS) is the nation's premier system of health-related telephone surveys that collect state data about U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. Established in 1984 with 15 states, BRFSS now collects data in all 50 states as well as the District of Columbia and three U.S. territories. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world. See More.

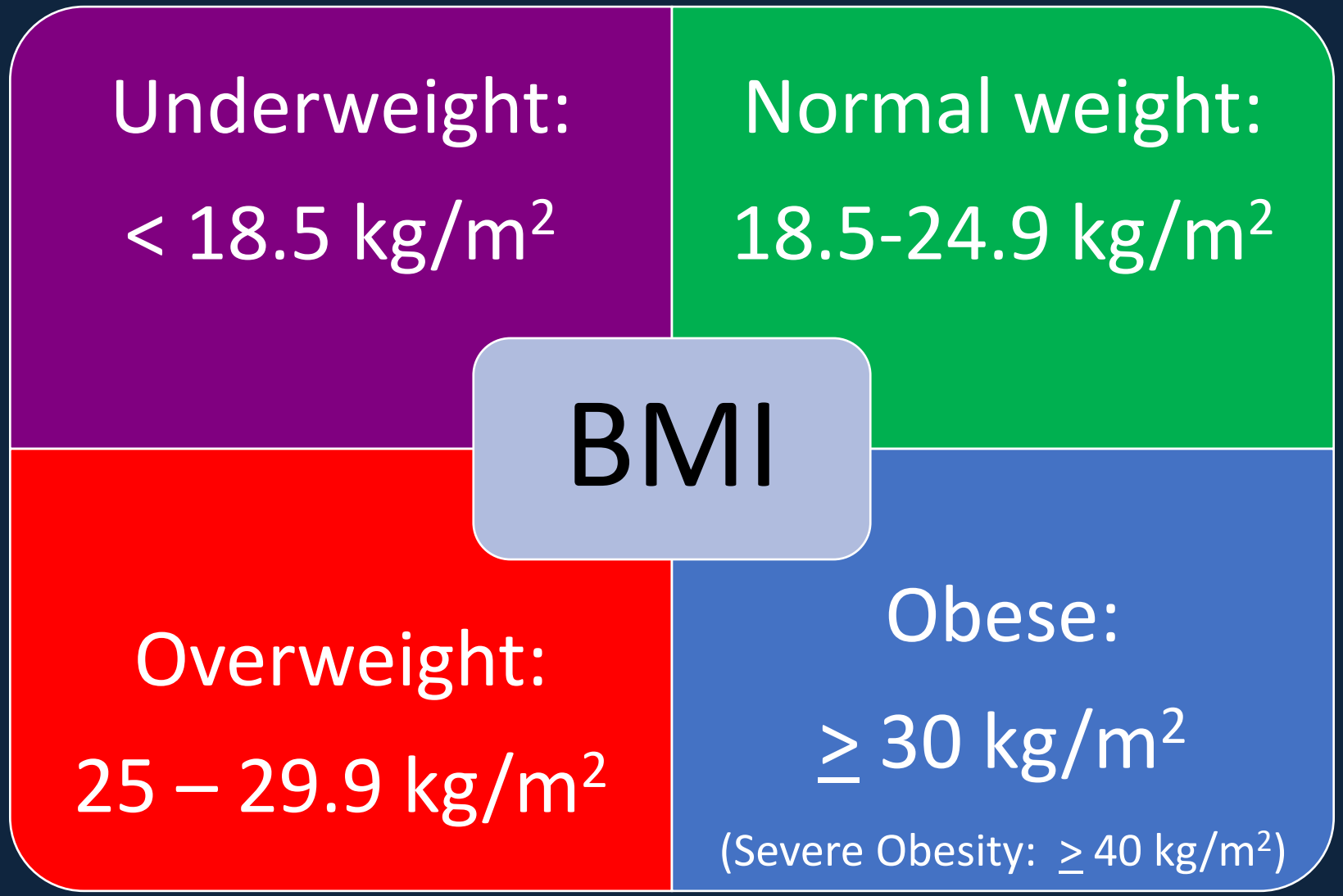
Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]

Summary Points

- ***Who***: Department of Health of PR with support of the WHO and PAHO
- ***What***: Prior 2 cycle data on obesity + an action plan for prevention of obesity in PR
- ***When***: 2016-2025
- ***Where***: Puerto Rico
- ***How***: "Detener el aumento acelerado en las tasas de prevalencia de obesidad en la población mediante la implantación de acciones multisectoriales"

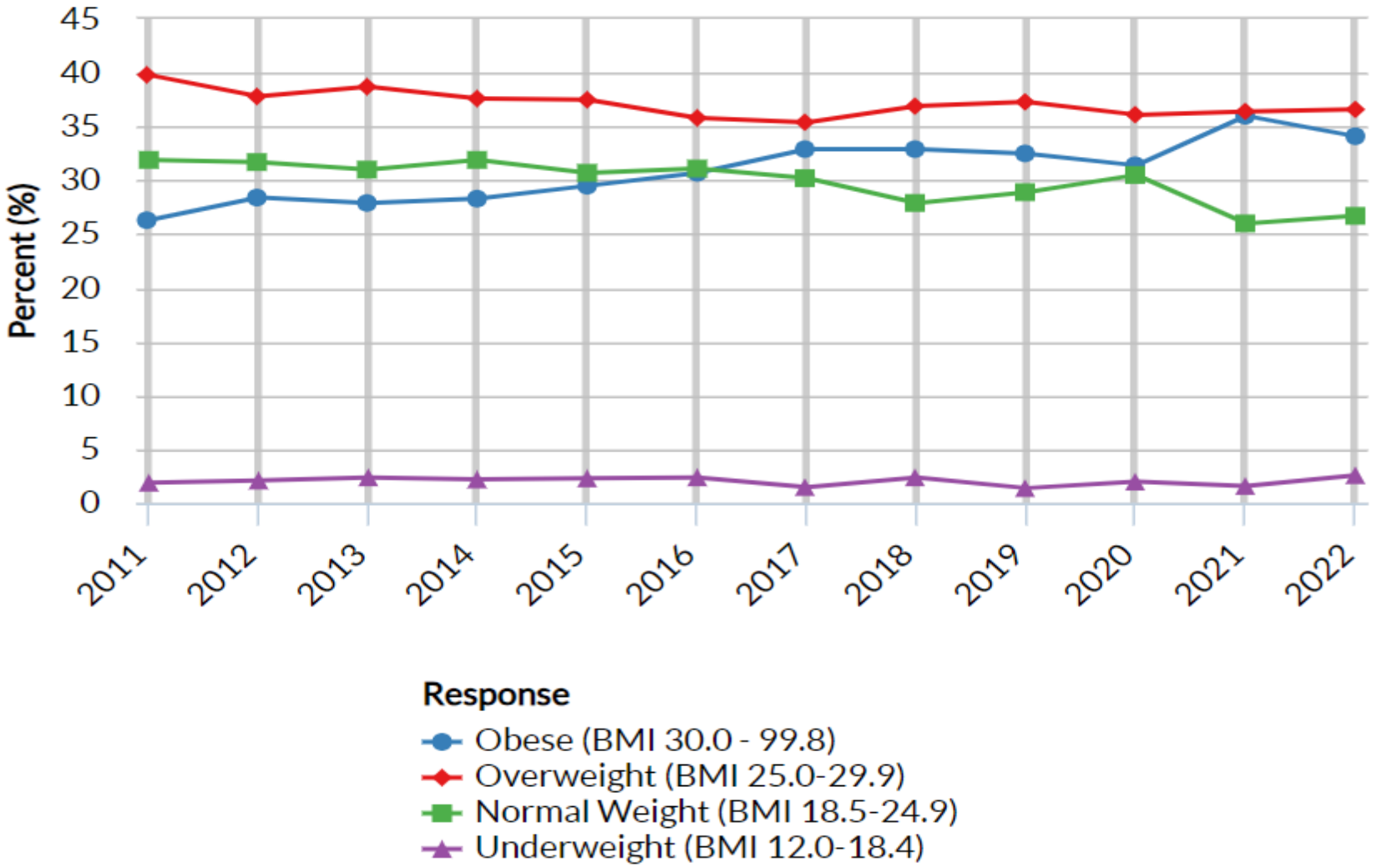


Comisión de Alimentación y Nutrición de Puerto Rico. (2023). Plan de Acción para la Prevención de la Obesidad en Puerto Rico 2023 - 2025. Departamento de Salud, San Juan, PR. Accessed July 20, 2024.



World Health Organization. Fact sheets: obesity and overweight. 1 March 2024. Accessed July 26, 2024. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight/
Centers for Disease Control and Prevention. Adult BMI Categories. 19 March 2024. Accessed July 27, 2024. https://www.cdc.gov/bmi/adult-calculator/bmi-categories.html/

Puerto Rico BMI 2011 - 2022



Data Source: Behavioral Risk Factor Surveillance System (BRFSS)

Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]

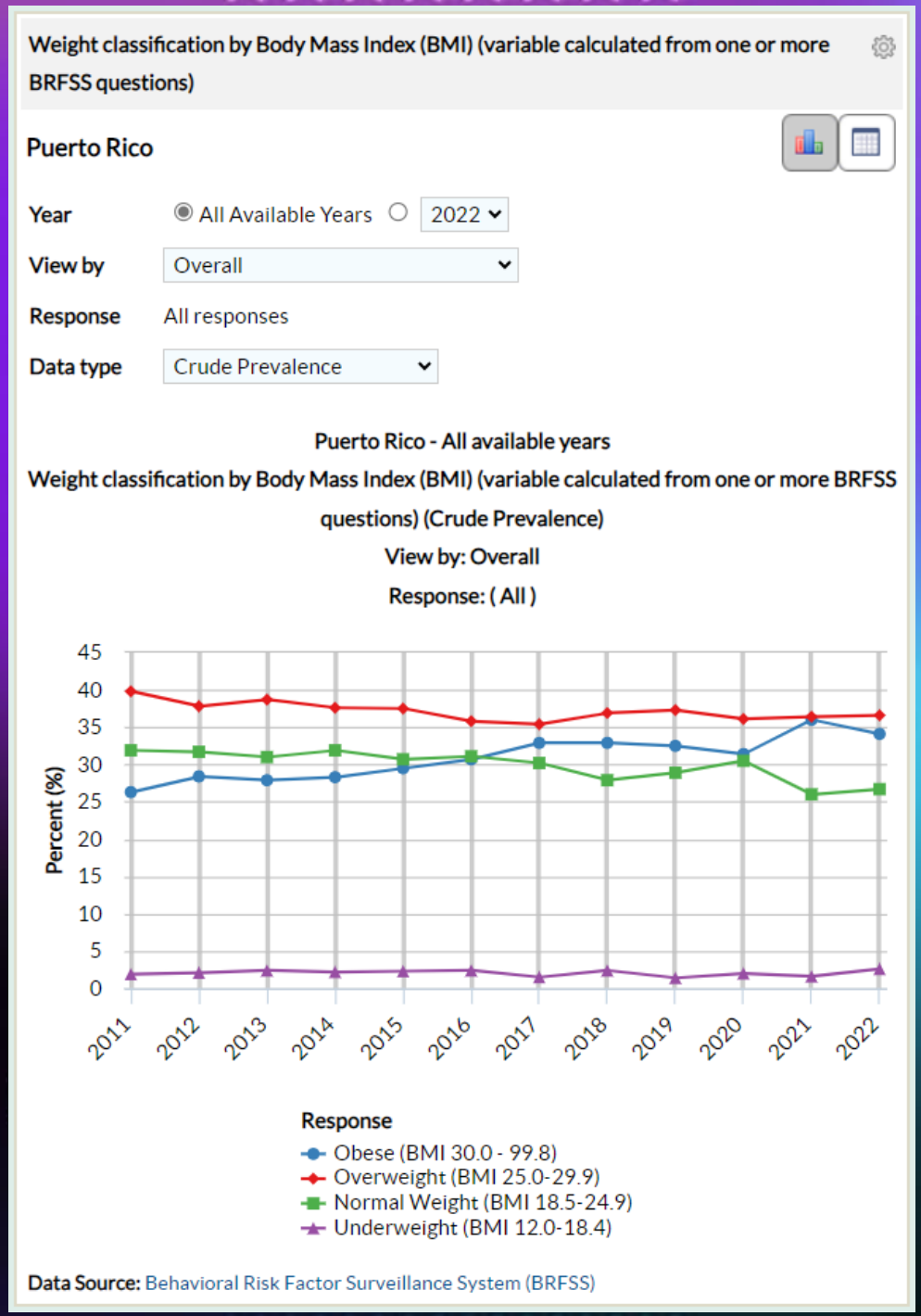
70.7% of the population of Puerto Rico have overweight or obesity (2022).

Obese: 34.1%

Overweight: 36.6%

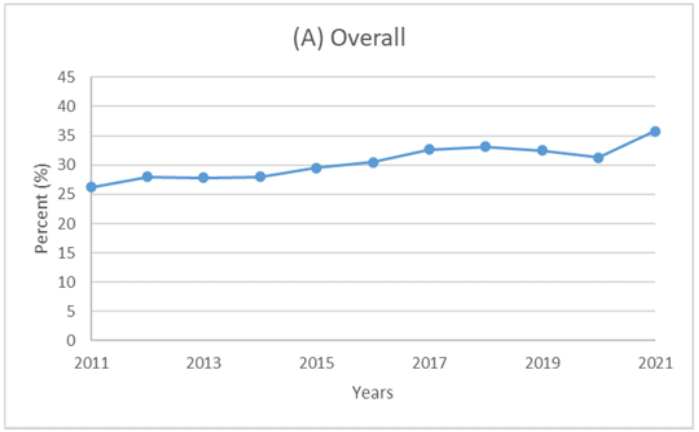
Normal weight: 26.7%

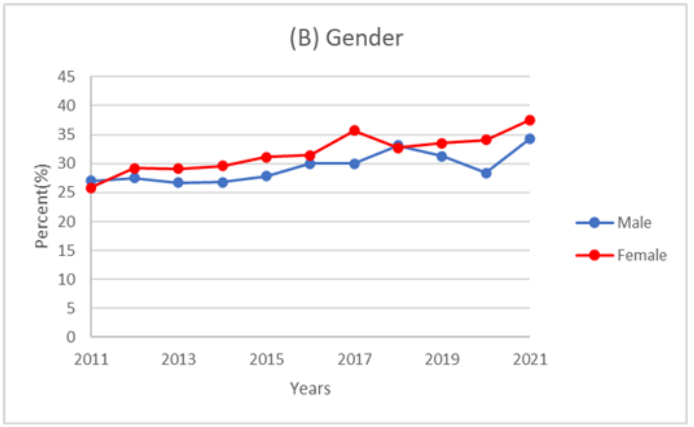
Underweight: 2.6%

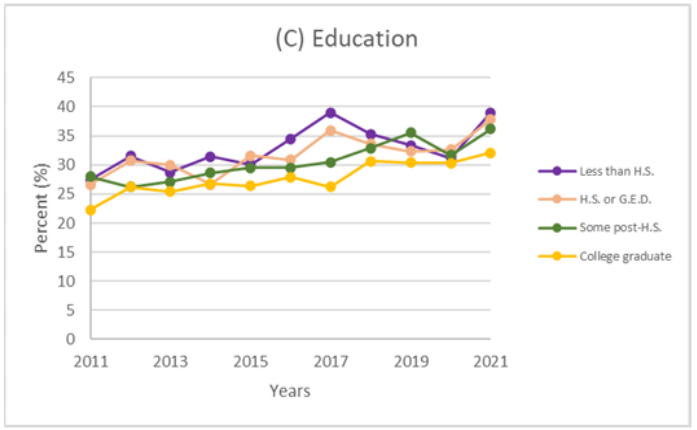


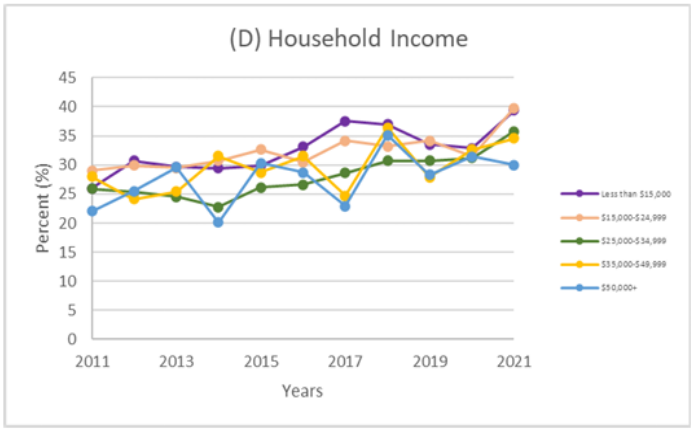
Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]

Figure 12: Age-adjusted prevalence estimates of Obese adults, Puerto Rico 2011-2021

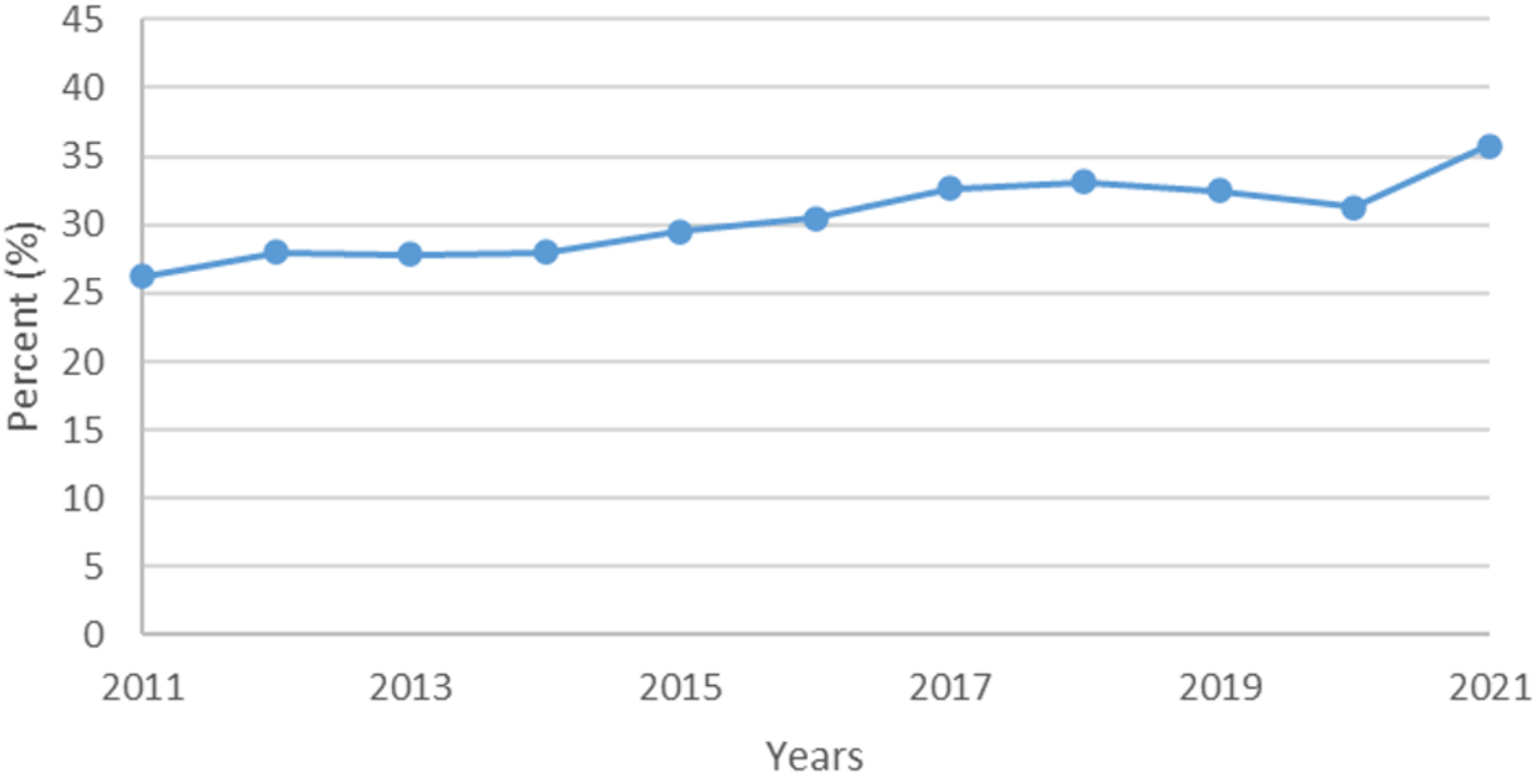








Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]



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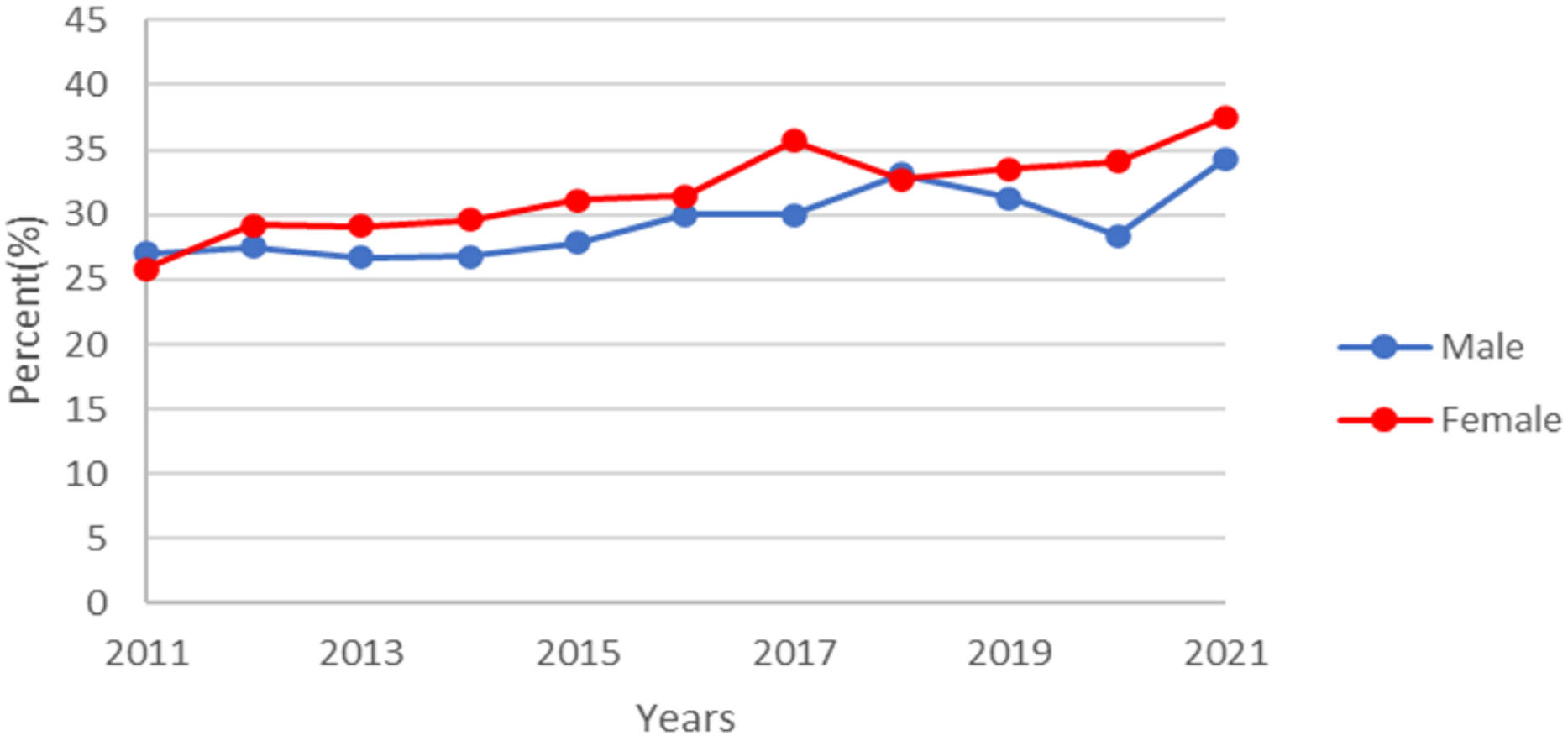

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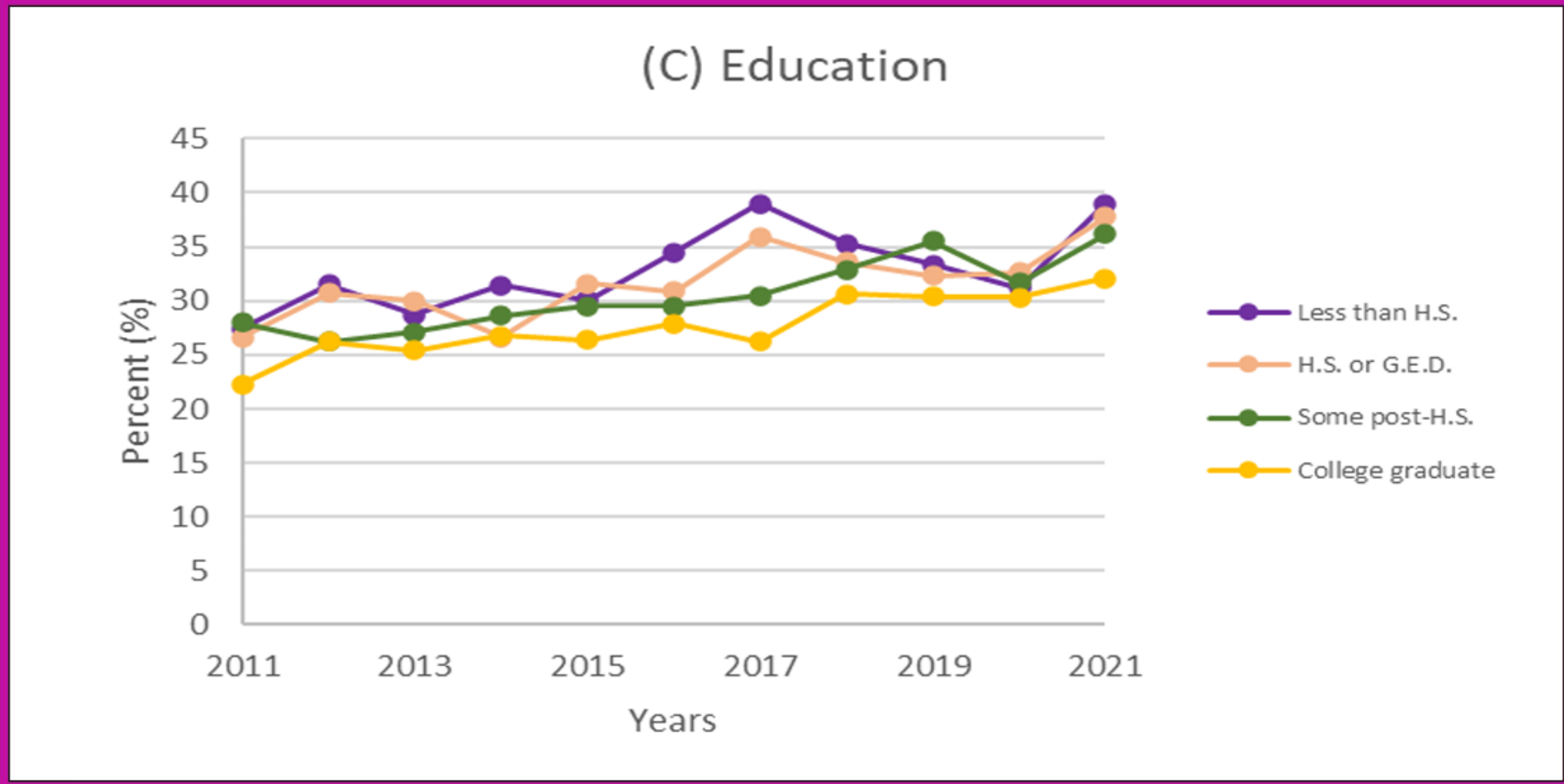

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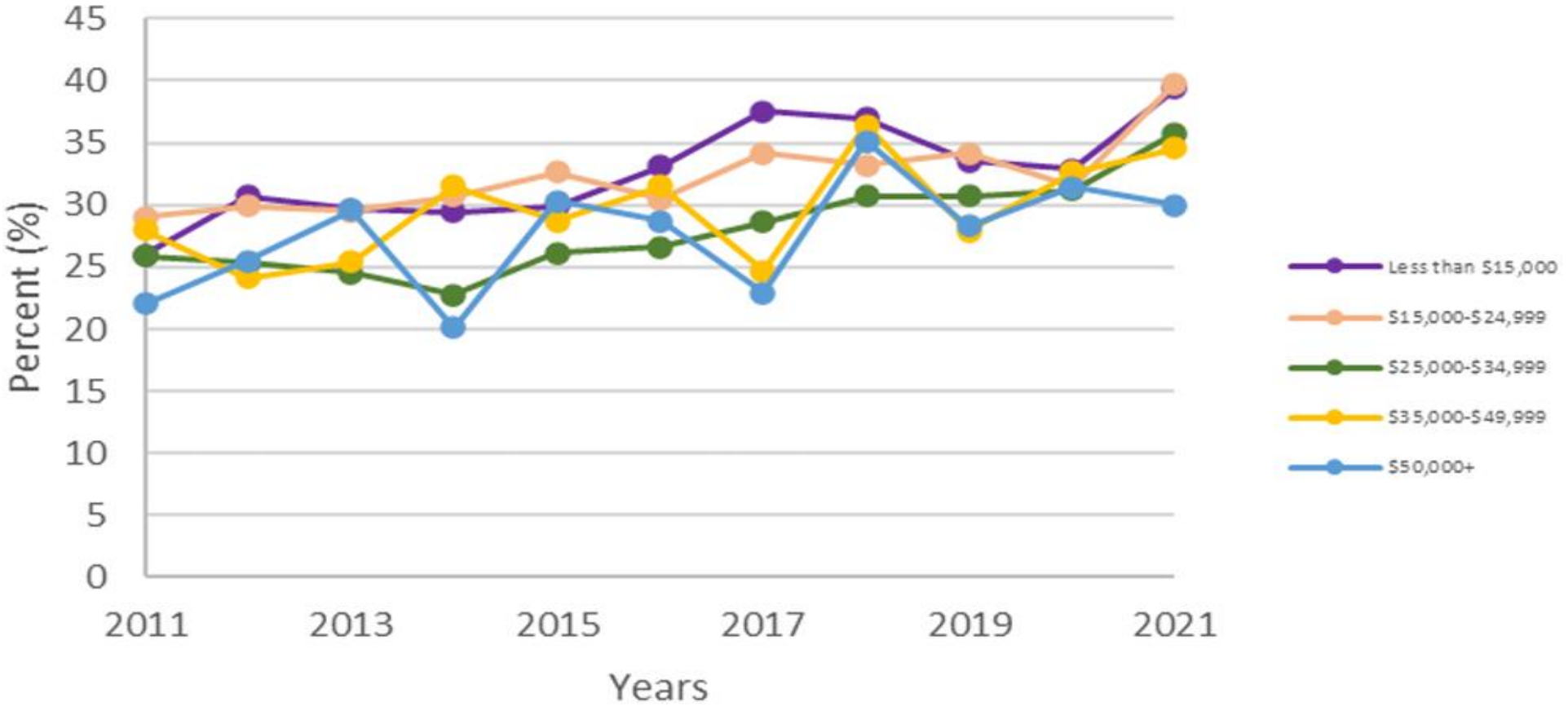
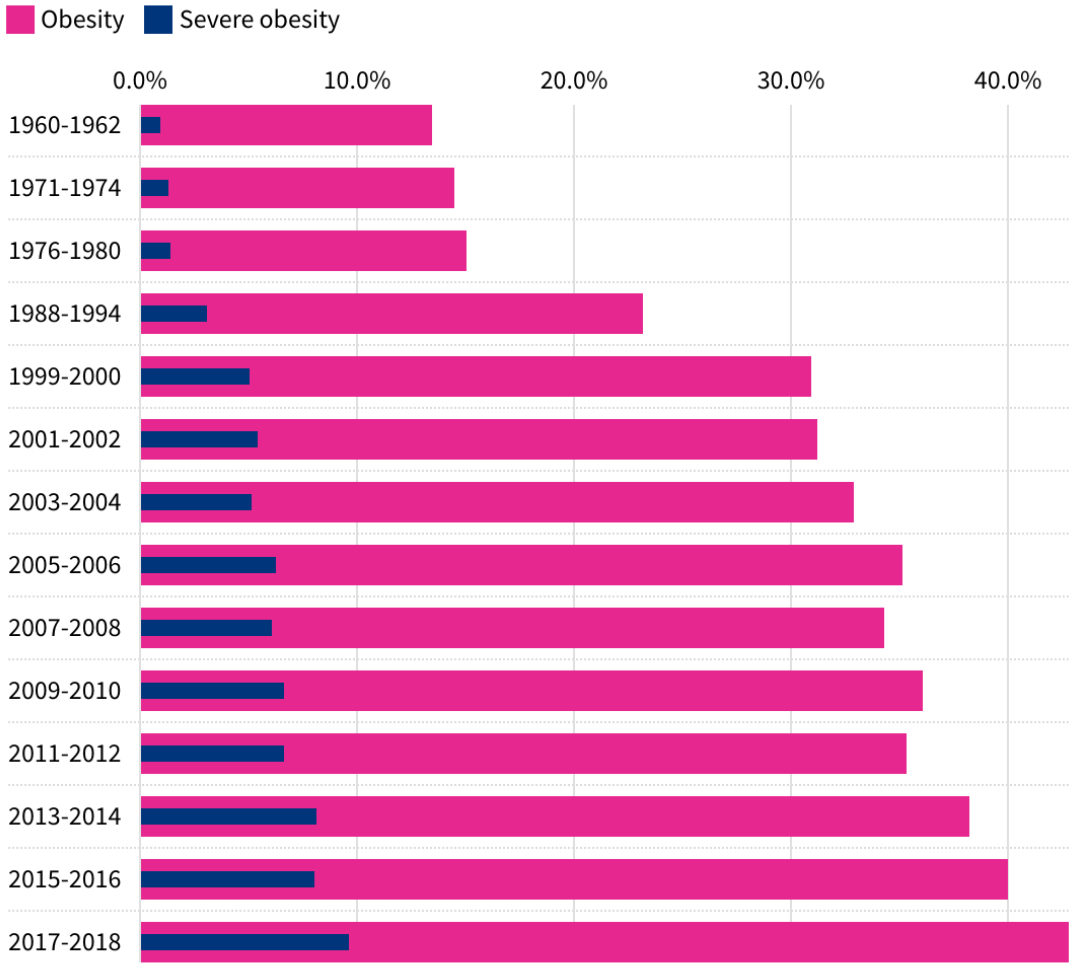


Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]

How does Puerto Rico compare with the United States?

Nationwide obesity rates have more than tripled since the 1960s.

Age-adjusted nationwide obesity and severe obesity rates according to National Health and Nutrition Examination Surveys



This accounts for the population between the ages of 20-74. The obesity category already includes severe obesity.

Source: Centers for Disease Control and Prevention, National Center for Health Statistics

USAFACTS

Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Jul 20, 2024]

U.S. Adults

- **73.6%** of adults 20+ YO have either overweight OR obesity (as of 2018)
- **41.9%** of adults in the US have obesity (as of March 2020)
  - 9.2% of adults in the US have severe obesity (BMI ≥ 40)
- Most affected groups:
  - Non-Hispanic Black adults
  - Adults with less education

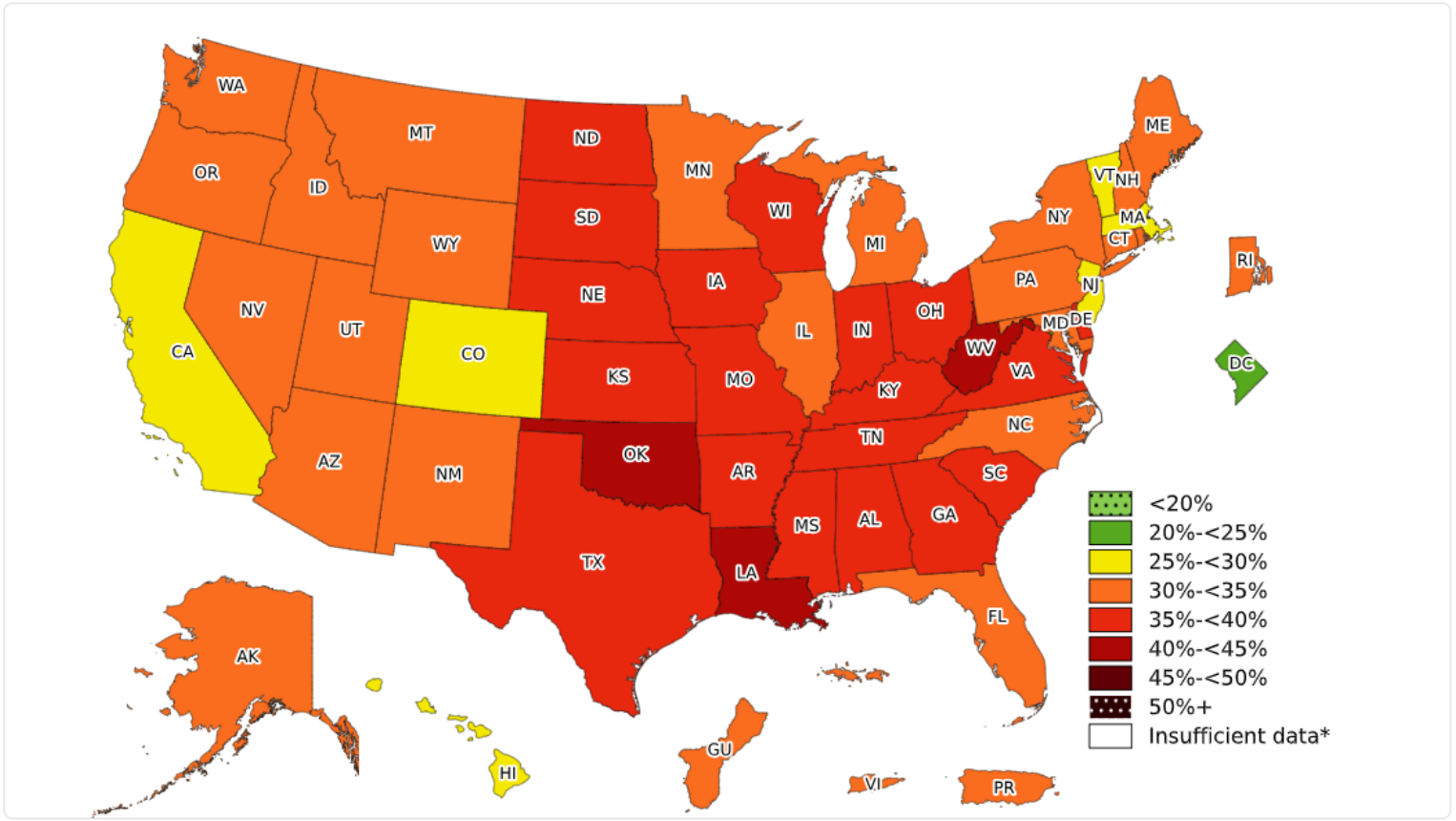
Centers for Disease Control and Prevention. National Center for Health Statistics. Obesity and Overweight. 5 January 2023. Accessed July 27, 2024. https://www.cdc.gov/nchs/fastats/obesity-overweight.htm/
Centers for Disease Control and Prevention. Adult Obesity Facts. 14 May 2024. Accessed July 27, 2024. https://www.cdc.gov/obesity/php/data-research/adult-obesity-facts.html/

U.S. Adolescents + Kids

- **22.2%** of adolescents aged 12-19 YO have obesity (as of March 2020)
- **20.7%** of children aged 6-11 YO have obesity (as of March 2020)
- **12.7%** of children aged 2-5 YO have obesity (as of March 2020)

Centers for Disease Control and Prevention. National Center for Health Statistics. Obesity and Overweight. 5 January 2023. Accessed July 27, 2024. https://www.cdc.gov/nchs/fastats/obesity-overweight.htm/
Centers for Disease Control and Prevention. Adult Obesity Facts. 14 May 2024. Accessed July 27, 2024. https://www.cdc.gov/obesity/php/data-research/adult-obesity-facts.html/

Map: Overall Obesity



In 2022, more than 1 in 5 adults in all U.S. states and territories had obesity.

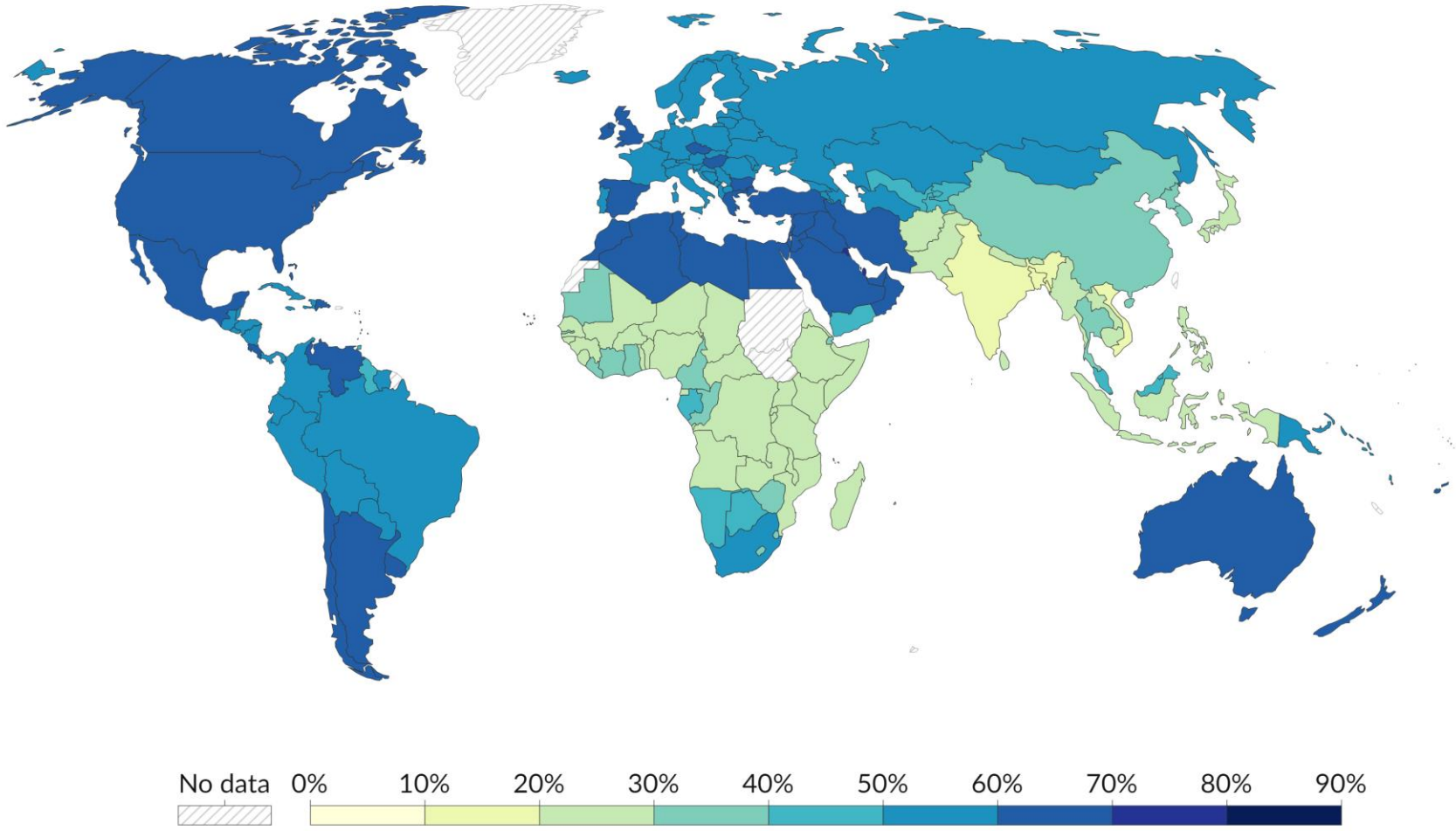
Source: Behavioral Risk Factor Surveillance System

Centers for Disease Control and Prevention. *Adult Obesity Prevalence Maps*. U.S. Dept of Health and Human Services; 2022.

Share of adults who are overweight or obese, 2016

"Overweight" is defined here as a body mass index (BMI) above 25. BMI is a person's weight in kilograms divided by their height in meters squared.

Our World in Data



Data source: World Health Organization - Global Health Observatory (2024)

OurWorldInData.org/obesity | CC BY

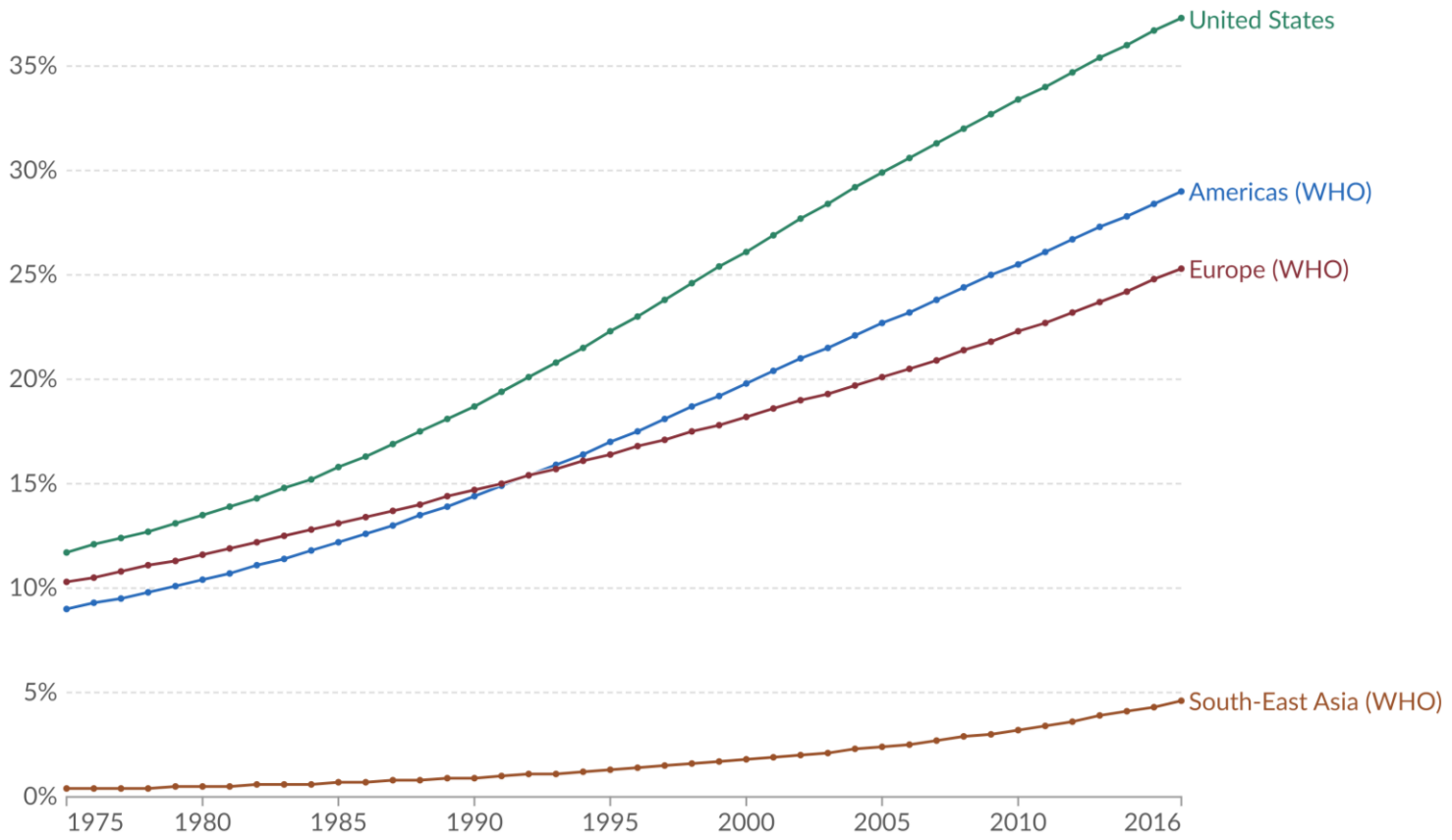
How does Puerto Rico compare with the world?

World Health Organization - Global Health Observatory (2024) – processed by Our World in Data. Open access under the Creative Commons By License.

Obesity in adults, 1975 to 2016

Our World in Data

Estimated prevalence of obesity[1], based on general population surveys and statistical modeling. Obesity is a risk factor[2] for chronic complications, including cardiovascular disease, and premature death.



Data source: WHO, Global Health Observatory (2022)

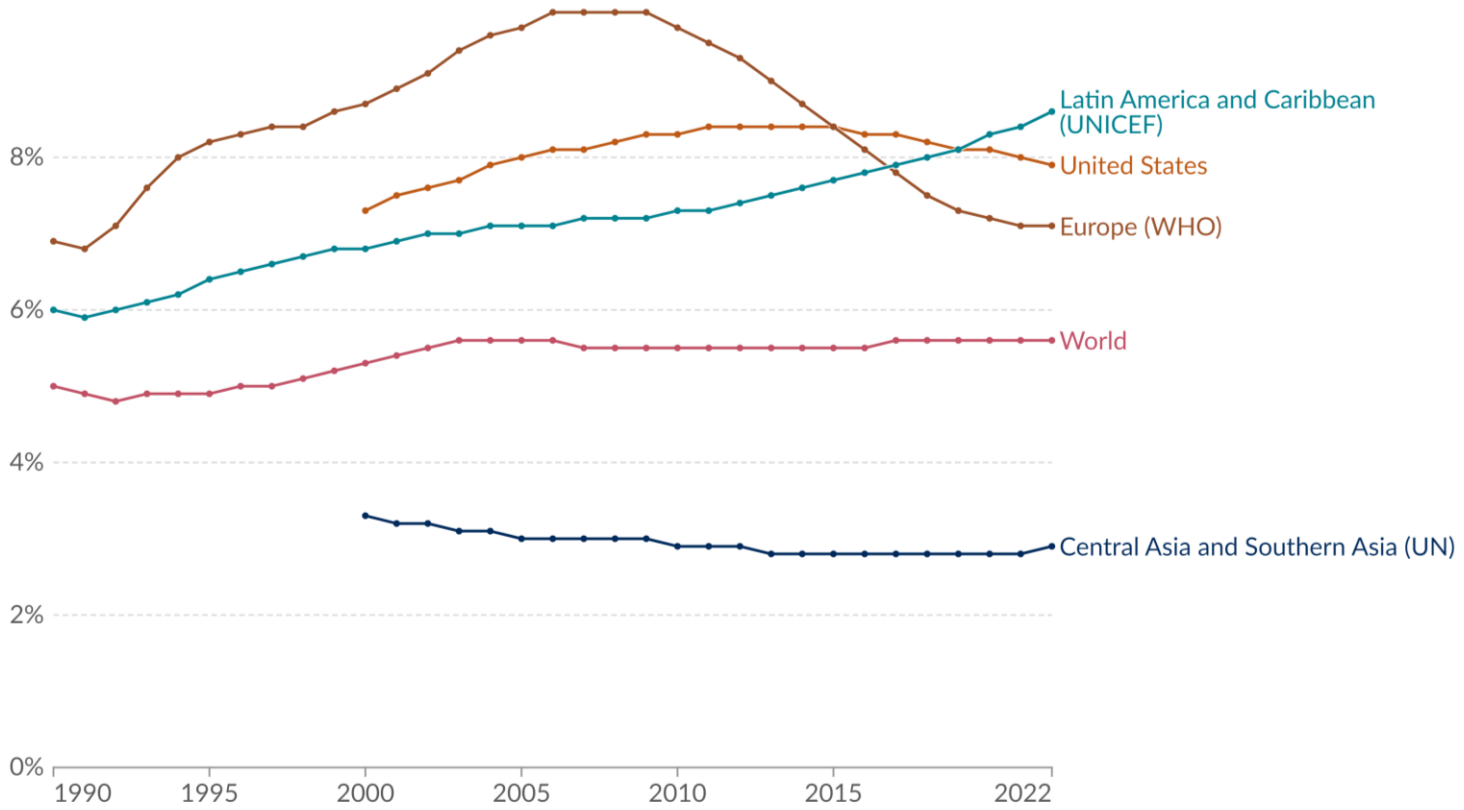
OurWorldInData.org/obesity | CC BY

World Health Organization - Global Health Observatory (2024) – processed by Our World in Data. Open access under the Creative Commons By License.

Share of children who are overweight or obese, 1990 to 2022

Our World in Data

Share of children under five years old that are defined as overweight or obese. A child is classified as overweight if their weight-for-height is more than two standard deviations from the median of the World Health Organization (WHO) Child Growth Standards.



Data source: WHO, Global Health Observatory (GHO)

OurWorldInData.org/obesity | CC BY

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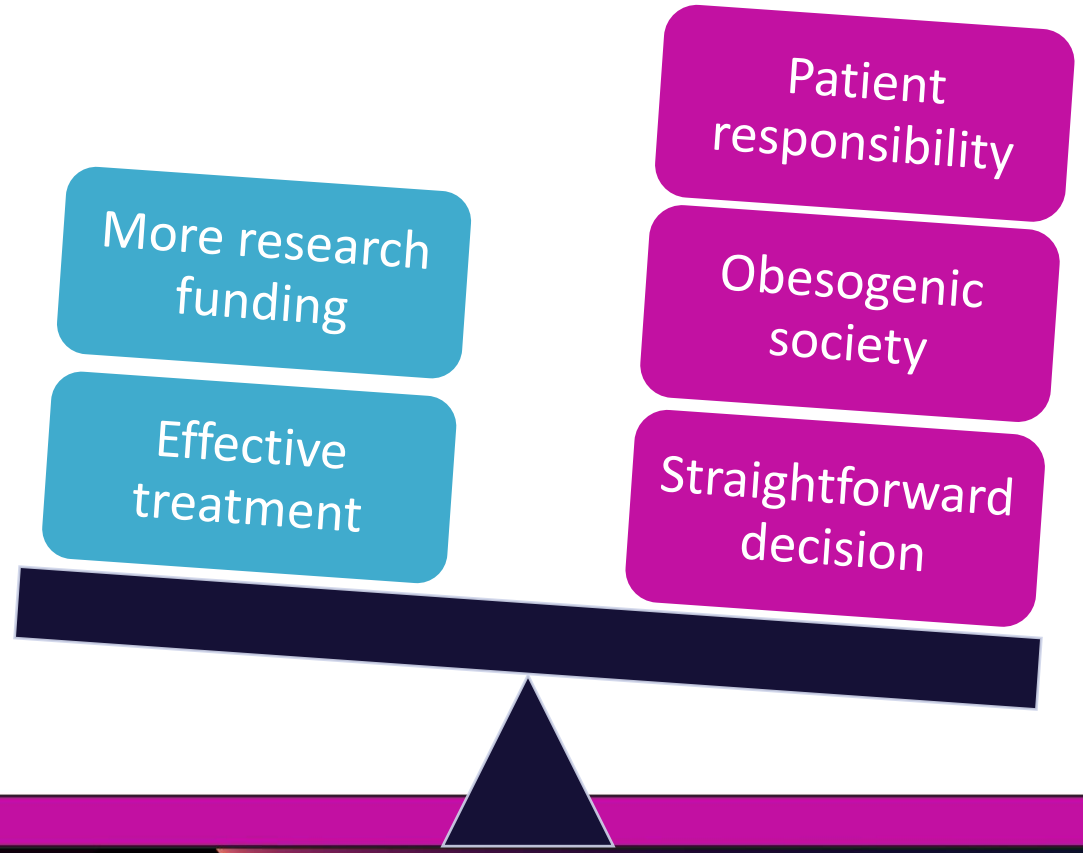
Group Activity

Obesity: *A Chronic Disease?* or *A Lifestyle Choice?*



AMA PolicyFinder

obesity

Search

Public Health

Recognition of Obesity as a Disease H-440.842

Topic: Public Health

Meeting Type: Annual

Policy Subtopic: NA

Year Last Modified: 2023

Our American Medical Association recognizes **obesity** as a disease state with multiple pathophysiological aspects requiring a range of interventions to advance **obesity** treatment and prevention.

Policy Timeline

Res. 420, A-13 Reaffirmed: CSAPH Rep. 08, A-23

As easy as 1+2 = 3?

Original Article
PEDIATRIC OBESITY

Obesity

Four-Year Behavioral, Health-Related Quality of Life, and BMI Outcomes from a Cluster Randomized Whole of Systems Trial of Prevention Strategies for Childhood Obesity

Steven Allender[1], Liliana Orellana[2], Nic Crooks[1], Kristy A. Bolton[1], Penny Fraser[1], Andrew Dwight Brown[1], Ha Le[1,3], Janette Lowe[4], Kayla de la Haye[5], Lynne Millar[6], Marjorie Moodie[1,3], Boyd Swinburn[7], Colin Bell[8], and Claudia Strugnell[1]

Audience Participation Question!

Allender S, Orellana L, Crooks N, et al. Four-Year Behavioral, Health-Related Quality of Life, and BMI Outcomes from a Cluster Randomized Whole of Systems Trial of Prevention Strategies for Childhood Obesity. *Obesity (Silver Spring)*. 2021;29(6):1022-1035

Causes of obesity are numerous!

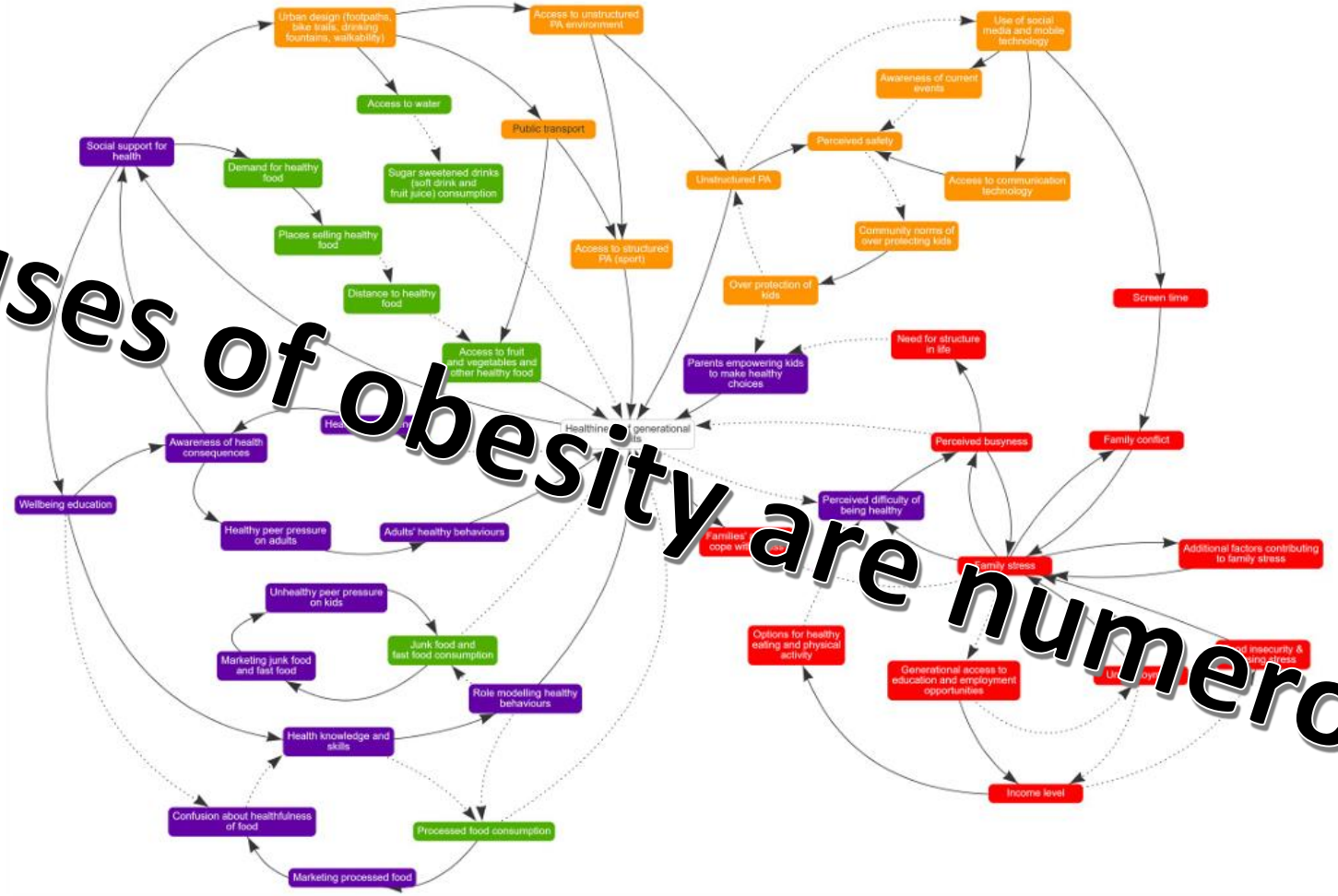
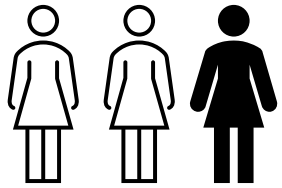
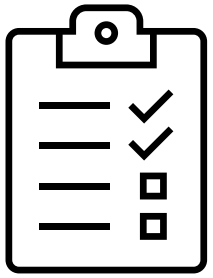


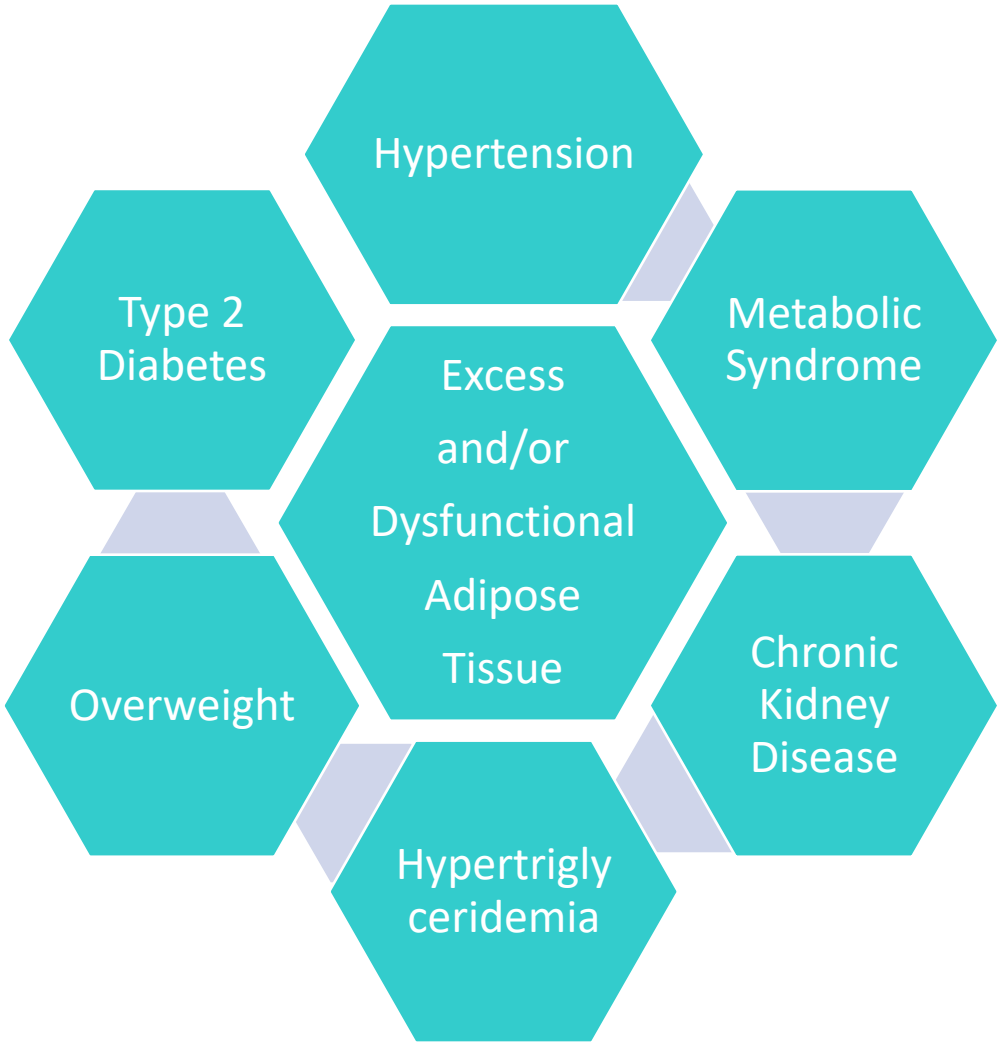
Figure 1 Community causal loop diagram of causes of obesity. PA, physical activity.

Allender S, Orellana L, Crooks N, et al. Four-Year Behavioral, Health-Related Quality of Life, and BMI Outcomes from a Cluster Randomized Whole of Systems Trial of Prevention Strategies for Childhood Obesity. *Obesity (Silver Spring)*. 2021;29(6):1022-1035

Risk Factors for CKM Syndrome

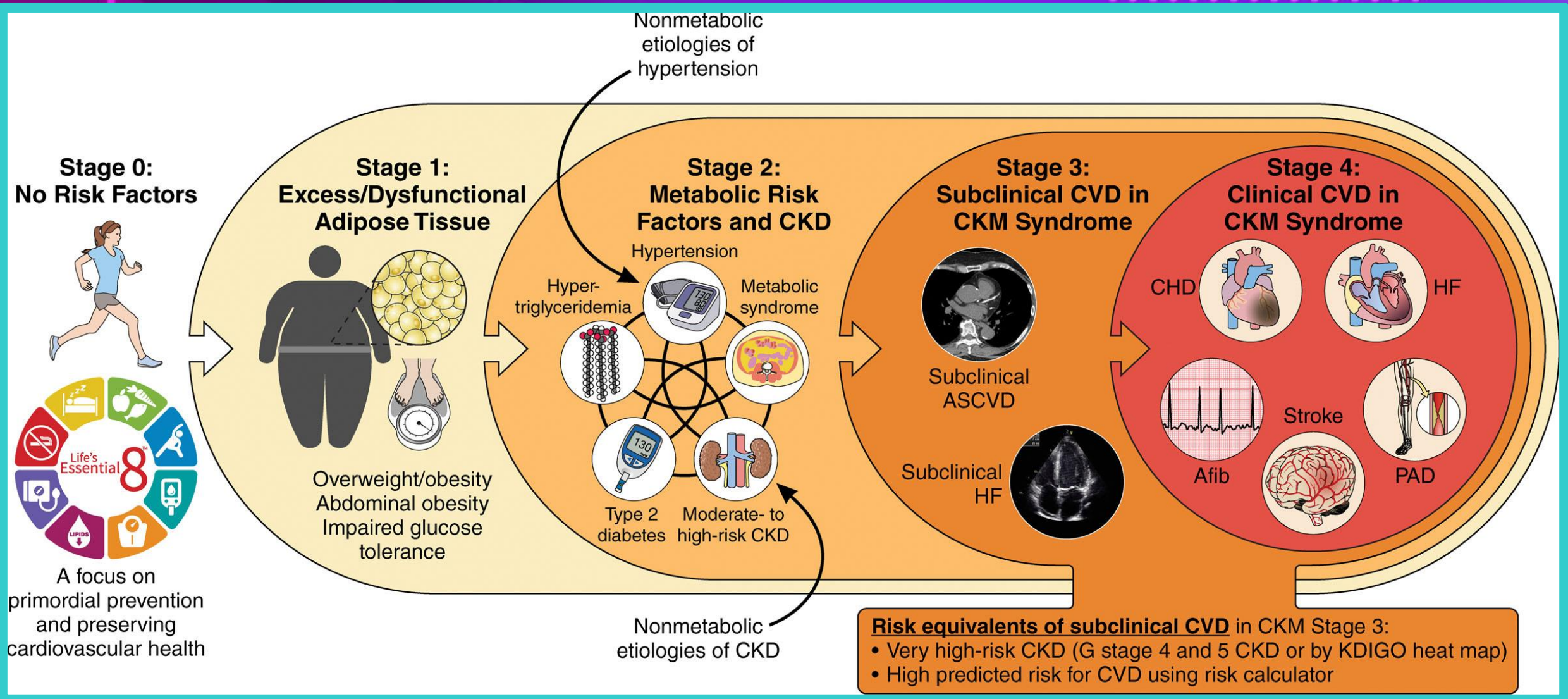






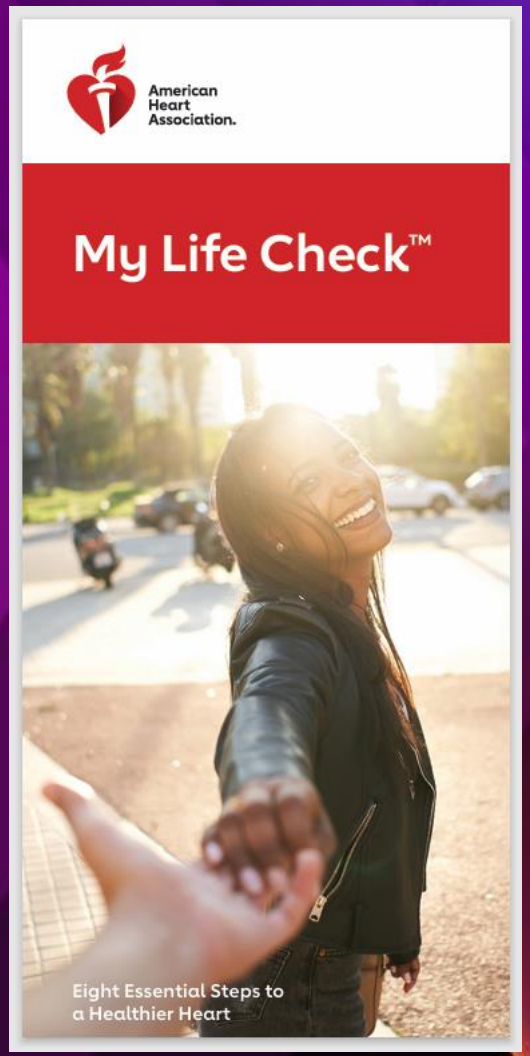
Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

Stages of CKM



Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

Audience Participation!



American Heart Association. My Life Check. my_life_check_brochure.pdf (heart.org)

Stages of CKM

Stage 0

- *No CKM risk factors*
- Normal: BMI, waist circumference, glucose, BP, lipids and no evidence of CKD or subclinical/clinical CVD

Stage 1

- *Excess or dysfunctional adiposity*
- Overweight/obese, abdominal obesity, dysfunctional adipose tissue **without** metabolic risk factors or CKD

Stage 2

- *Metabolic risk factors and CKD*
- Triglycerides ≥ 135 mg/dL, hypertension, metabolic syndrome, diabetes, or CKD

Stage 3

- *Subclinical CVD in CKM*
- Subclinical ASCVD or subclinical HF **with** excess/dysfunctional adiposity, CKM risk factors, or CKD

Stage 4

- *Clinical CVD in CKM*
- Clinical CVD (coronary heart disease, HF, stroke, PAD, AF) **with** excess/dysfunctional adiposity, CKM risk factors or CKD

Ndumele CE, Rangaswami J, Chow SL, et al.Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation*. 2024;149(13):e1023.

Stages of CKM

KDIGO Guideline Definition of CKD

CKD is classified based on:
- **Cause (C)**
- **GFR (G)**
- **Albuminuria (A)**

GFR categories (ml/min/1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314.

“An ounce of **prevention** is worth a pound of *cure*.”

PREVENT Equation

- AHA **PRE**dicting Risk of C**V**D E**VENT**s
- A calculator for providers to use to help predict patient risk
- PREVENT models were based on a total of 46 observational cohort studies and EMR datasets, which included 6,612,004 US adults 30-79 years of age
- The high concordance in risk estimates identified for ASCVD and HF (correlation ≥0.9) in the PREVENT equations supports the approach of estimating total CVD as a composite

Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(24):1982-2004.

Exclusion of Race in PREVENT

- It was decided not to include race as a predictor in the development of PREVENT and to use the recently developed race-free equations for eGFR on the basis of serum creatinine (CKD-EPI 2021 [Chronic Kidney Disease Epidemiology Collaboration]).
- This is consistent with the growing consensus to remove the use of race from clinical algorithms broadly in medicine
- **Racism, <u>not race</u>, structures our social and individual lived experiences, is associated with adverse SDOH, and represents a key driver of adverse CVD outcomes**
- Calibration of PREVENT across key sociodemographic subgroups (eg, race and ethnicity, strata of social deprivation index) was carefully assessed and demonstrated good calibration among Black individuals

Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(24):1982-2004.

PREVENT Equation

Screen for CKM Risk

- Assess Life's Essential 8 (dietary patterns, physical activity, sleep duration and quality, nicotine exposure, body mass index, blood pressure, lipids, and blood sugar)
- Consider additional testing as clinically indicated: HbA1c, UACR, etc.

Assess CVD Risk

Among adults aged 30-79 y

- Calculate: 10- and 30-y absolute risk of CVD, ASCVD, and HF with PREVENT
- Personalize: In the setting of a clinician-patient discussion, consider risk-enhancing factors for shared decision-making
- Reclassify: In those at intermediate risk or when there is uncertainty, consider sequential testing with biomarkers or imaging

Determine CKM Stage

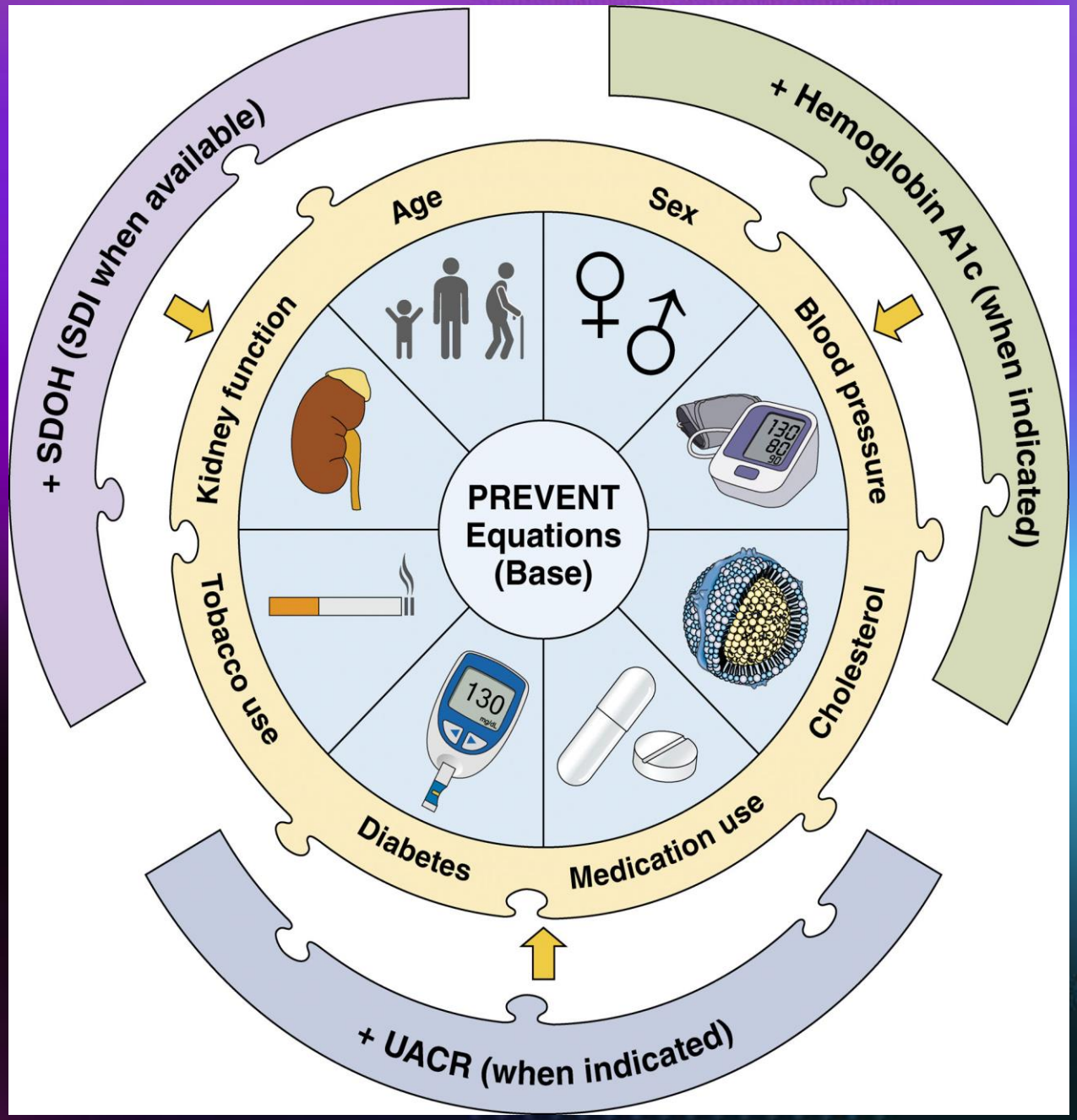
- CKM Stage 0: No CKM risk factors
- CKM Stage 1: Excess or dysfunctional adiposity
- CKM Stage 2: Metabolic risk factors or CKD
- CKM Stage 3: Subclinical CVD, very high-risk CKD, or high predicted CVD risk by PREVENT
- CKM Stage 4: Clinical CVD

Reduce CKM Risk

- Promote CKM health, prevent CKM progression, prioritize CKM regression
- Treat CKM factors and consider cardioprotective therapies according to guideline recommendations when indicated (eg, statin, SGLT2i, GLP-1RA)
- Screen for and address adverse SDOH
- Reassess CKM factors at guideline-recommended intervals

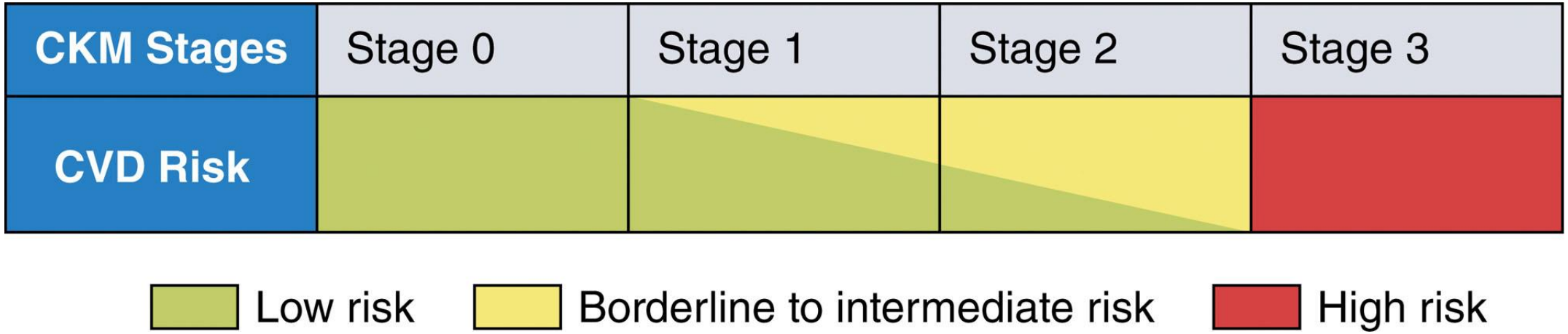
Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(24):1982-2004.

PREVENT base and additional equations:



Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(24):1982-2004.

PREVENT Risk Estimates



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PREVENT™ Online Calculator

Welcome to the American Heart Association **Predicting Risk of cardiovascular disease EVENTs** (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

Sex ◉ Male ○ Female

Age

30-79 years

Total Cholesterol

130-320 mg/dL

Khan SS, Matsushita K, Sang Y, et al. Development and Validation of the American Heart Association Predicting Risk of Cardiovascular Disease EVENTs (PREVENT™) Equations. *Circulation* 2023.
Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. *Circulation*. 2023;148(24):1982-2004.

Grab your phones!

Audience Participation!

Case

LC is a 66-year-old female with a past medical history significant for: hypertension, diabetes, chronic kidney disease, and obesity. She comes to your primary care clinic today concerned about her risk for cardiovascular disease as her mother just passed away from a heart attack. The following labs/vitals were done today:

BMI 31kg/m^2 BP 139/72
TC 198 LDL 141 HDL 43.2 TG 53
SCr 1.34mg/dL eGFR 55ml/min

SCAN ME

Case

How would you classify LC's estimated 10-year risk of cardiovascular disease (CVD)?

A. Low risk < 5%
B. Borderline risk 5% - 7.4%
C. Intermediate risk 7.5% - 19.9%
D. High risk ≥ 20%

Case

How would you classify LC's estimated 10-year risk of cardiovascular disease (CVD)?

A. Low risk < 5%
B. Borderline risk 5% - 7.4%
C. Intermediate risk 7.5% - 19.9%
D. High risk ≥ 20%

Case

Given LC's estimated 10-year risk of cardiovascular disease (CVD) of 23.5%, using share-decision making which of the following medications could be considered?

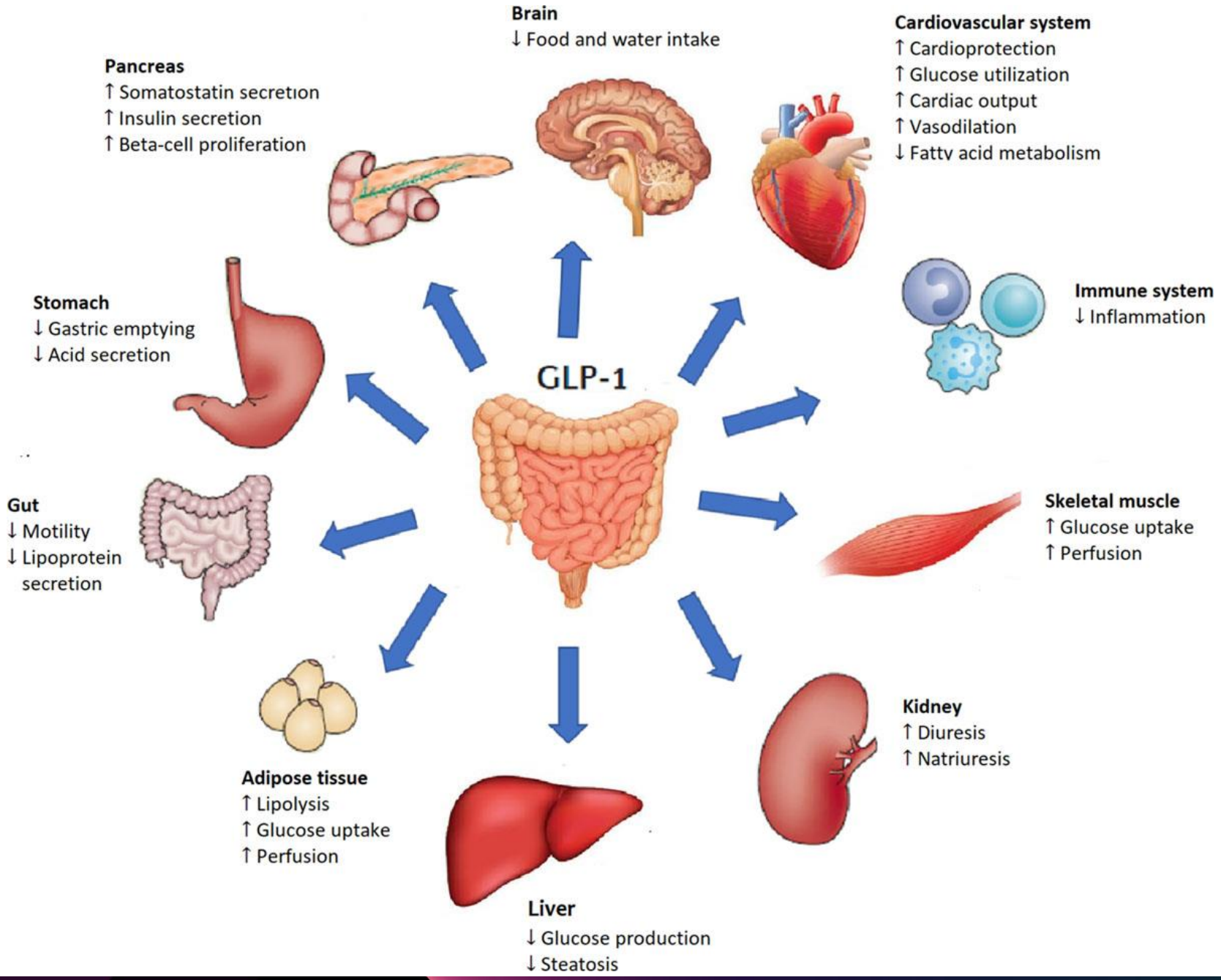
A. Empagliflozin 10mg daily
B. Lisinopril 5mg daily
C. Semaglutide 0.25 mg SC weekly
D. I don't know that's why I'm here…

SCAN ME

GLP-1 Receptor Agonists and SGLT-2 Inhibitors Use

	T2DM - Glycemic Control		MACE Risk Reduction		Prevention of HF		HF Hospitalization in Established HF Patients	
	SGLT2i	GLP-1 RA	SGLT2i	GLP-1 RA	SGLT2i	GLP-1 RA	SGLT2i	GLP-1 RA
T2DM Without Other Risk Factors	Y	Y	Trials needed@	Trials needed@	Trials needed@	Trials needed@	N/A	N/A
T2DM with Risk Factors	Y	Y	Mixed Results$	Mixed Results$	Y	Potential benefit #	N/A	N/A
T2DM with Established ASCVD/High Risk for HF	Y	Y	Y	Y	Y	Potential benefit #	N/A	N/A
T2DM with CKD	Y	Y	Y	Mixed results	Y	Potential benefit#	N/A	N/A
T2DM with Established HFrEF	Y	No (additional trials needed)&	Limited Data*	No (additional trials needed)&	N/A	N/A	Y	No (additional trials needed)
T2DM with Established HFpEF	Y^	Y^	Probably yes /insufficient data$	Probably yes /insufficient data$	N/A	N/A	Trials needed (underway)	Trials needed

Khan MS, Fonarow GC, McGuire DK, et al. Glucagon-Like Peptide 1 Receptor Agonists and Heart Failure: The Need for Further Evidence Generation and Practice Guidelines Optimization. *Circulation*. 2020;142(12):1205-1218.



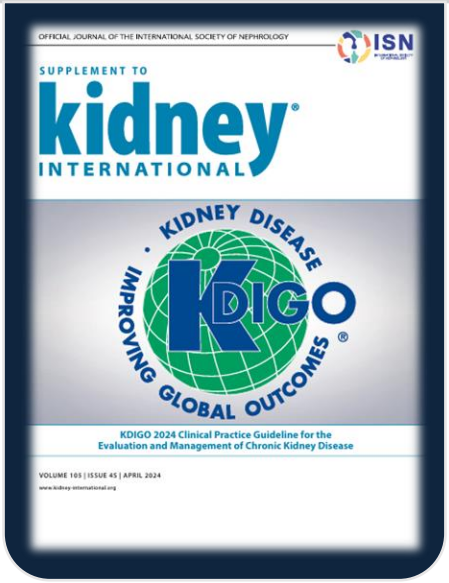
Khan MS, Fonarow GC, McGuire DK, et al. Glucagon-Like Peptide 1 Receptor Agonists and Heart Failure: The Need for Further Evidence Generation and Practice Guidelines Optimization. *Circulation*. 2020;142(12):1205-1218.

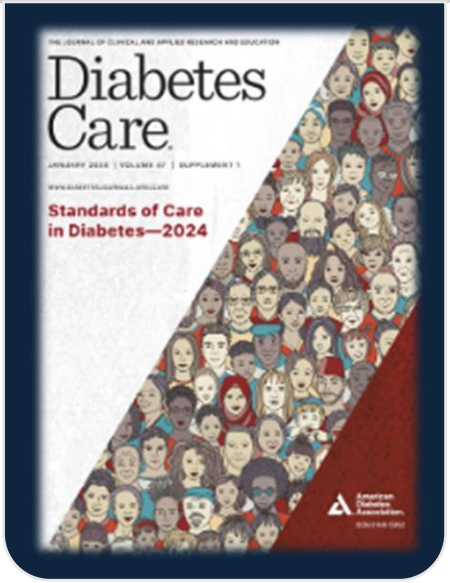
What do the guidelines say?

Cardio-vascular Disease

Chronic Kidney Disease

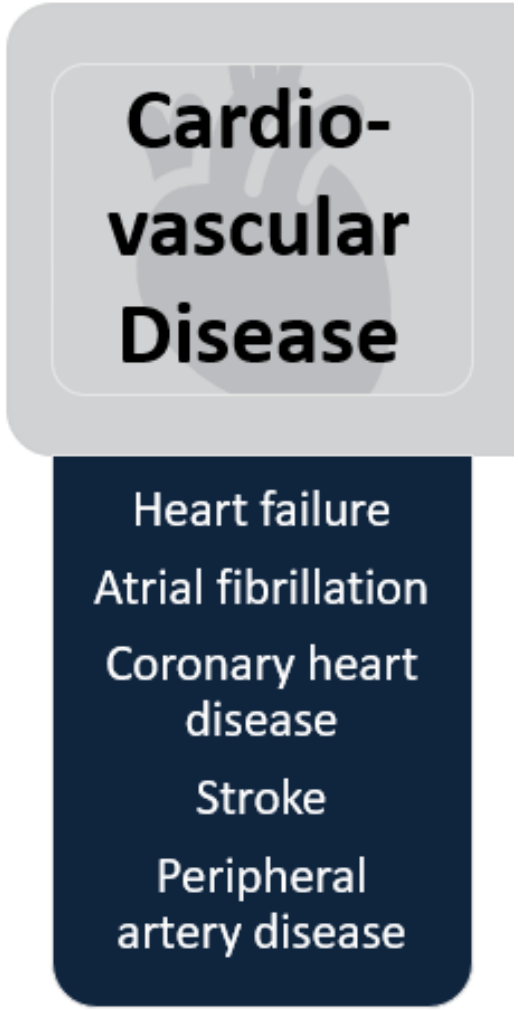
Diabetes and Obesity





Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314.
American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

Cardiovascular Guidelines



2024

Lower Extremity Peripheral Artery Disease
JACC | PDF | Hub **NEW!**

Hypertrophic Cardiomyopathy
JACC | PDF | Hub **NEW!**

2023

Atrial Fibrillation
JACC | PDF | Hub

Chronic Coronary Disease
JACC | PDF | Hub

2022

Aortic Disease
JACC | PDF | Hub

Heart Failure
JACC | PDF | Hub

2021

Coronary Artery Revascularization
JACC | PDF | Hub

Chest Pain
JACC | PDF | Hub

2020

Valvular Heart Disease
JACC | PDF | Hub

2019

Innovations, Modifications, and Evolution of ACC/AHA Clinical Practice Guidelines
JACC | PDF | News Story

Primary Prevention
JACC | PDF | Hub

https://www.acc.org/Guidelines

SGLT2i + GLP1a: Place in Therapy

Lifestyle therapy

Physical activity
Nutrition
Weight loss

With DM

First-line therapy

Metformin

eGFR < 45	eGFR < 30	Dialysis
Reduce dose	Discontinue	Discontinue

+

SGLT2 inhibitor

eGFR < 20	Dialysis
Do not initiate	Discontinue

GLP-1 receptor agonist (preferred)

DPP-4 inhibitor | **Insulin**

Sulfonylurea | **TZD**

Alpha-glucosidase inhibitor

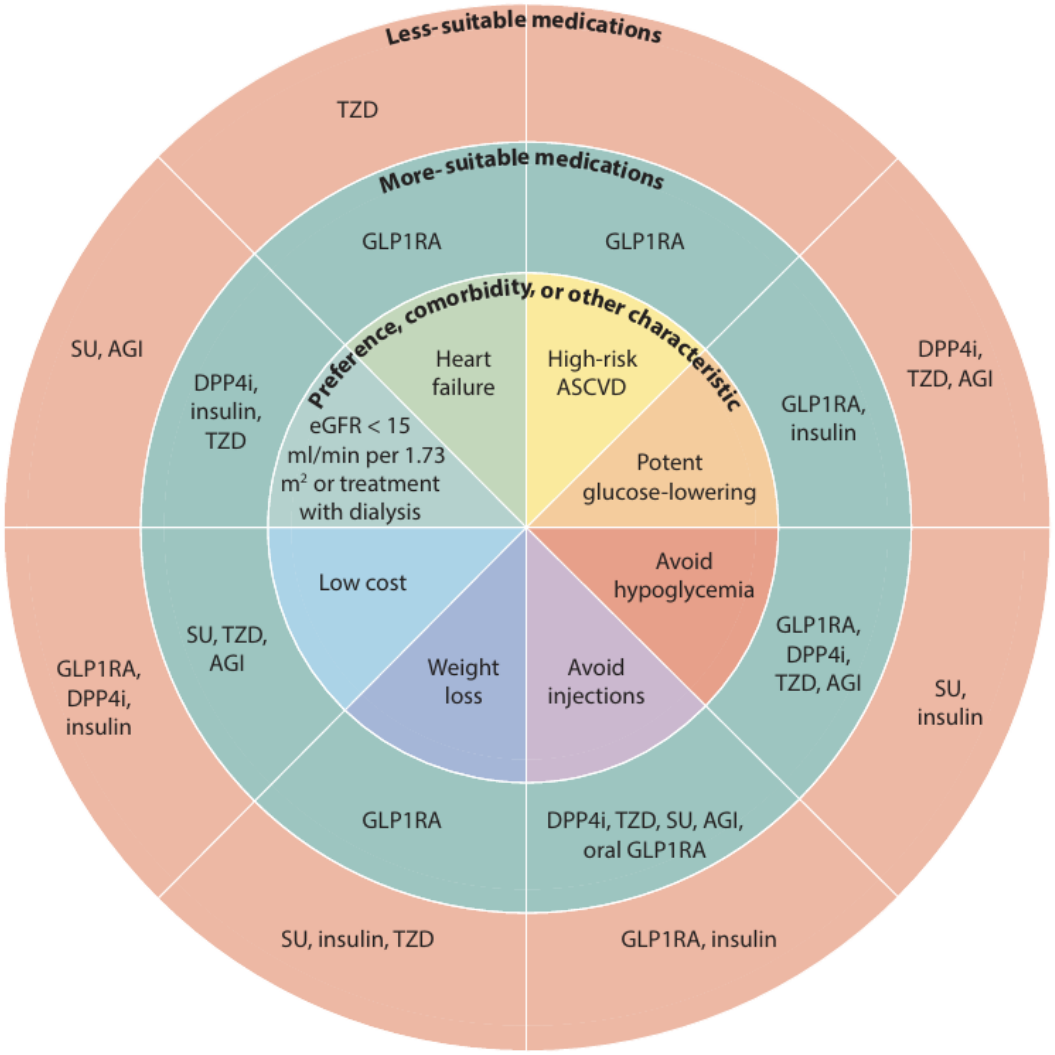
Additional drug therapy as needed for glycemic control

- Guided by patient preferences, comorbidities, eGFR, and cost
- Includes patients with eGFR < 30 ml/min per 1.73 m^2 or treated with dialysis
- See Figure 25

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in of Chronic Kidney Disease. *Kidney Int*. 2022;102(5S):S1-S127.

SGLT2i + GLP1a: Place in Therapy

With DM



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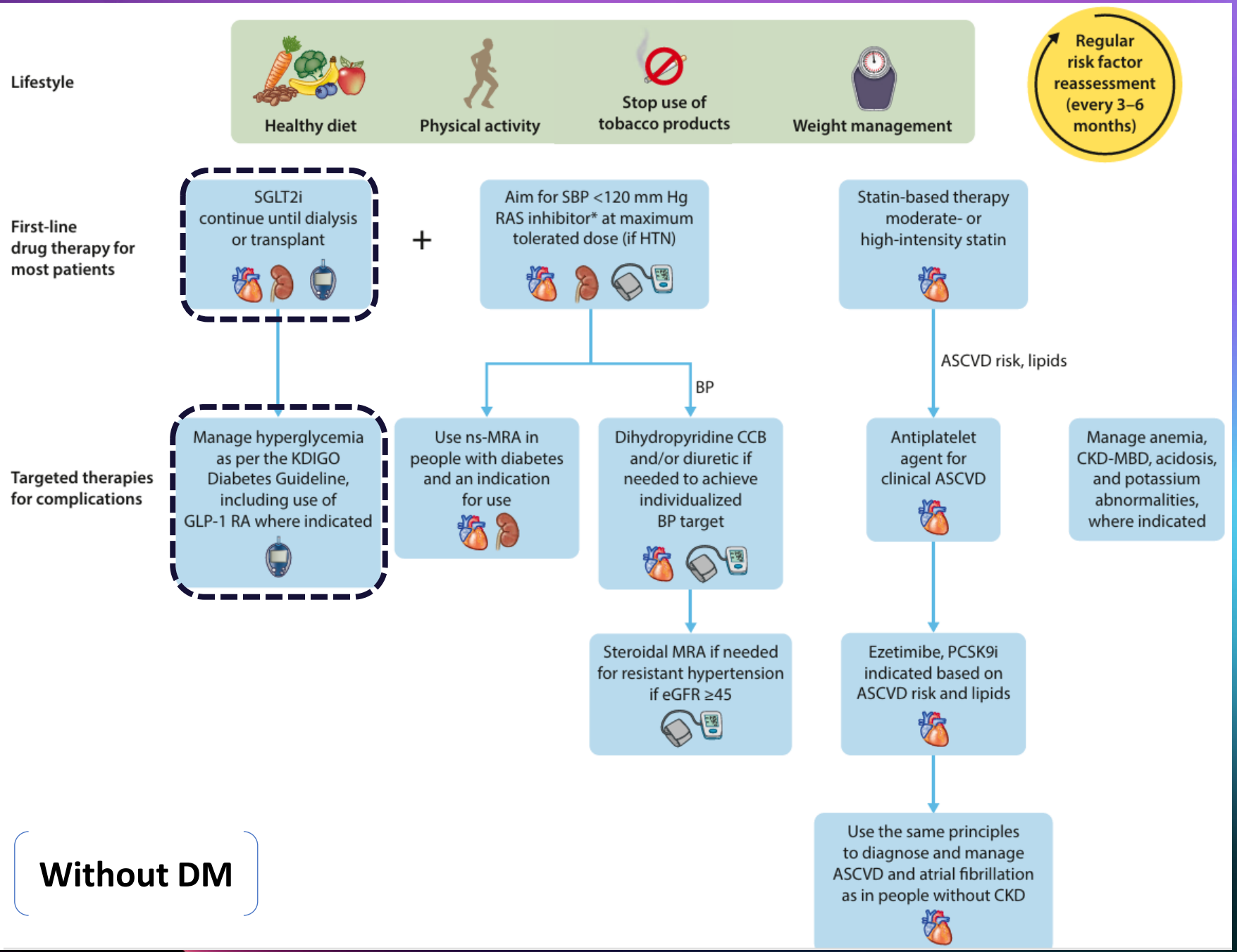
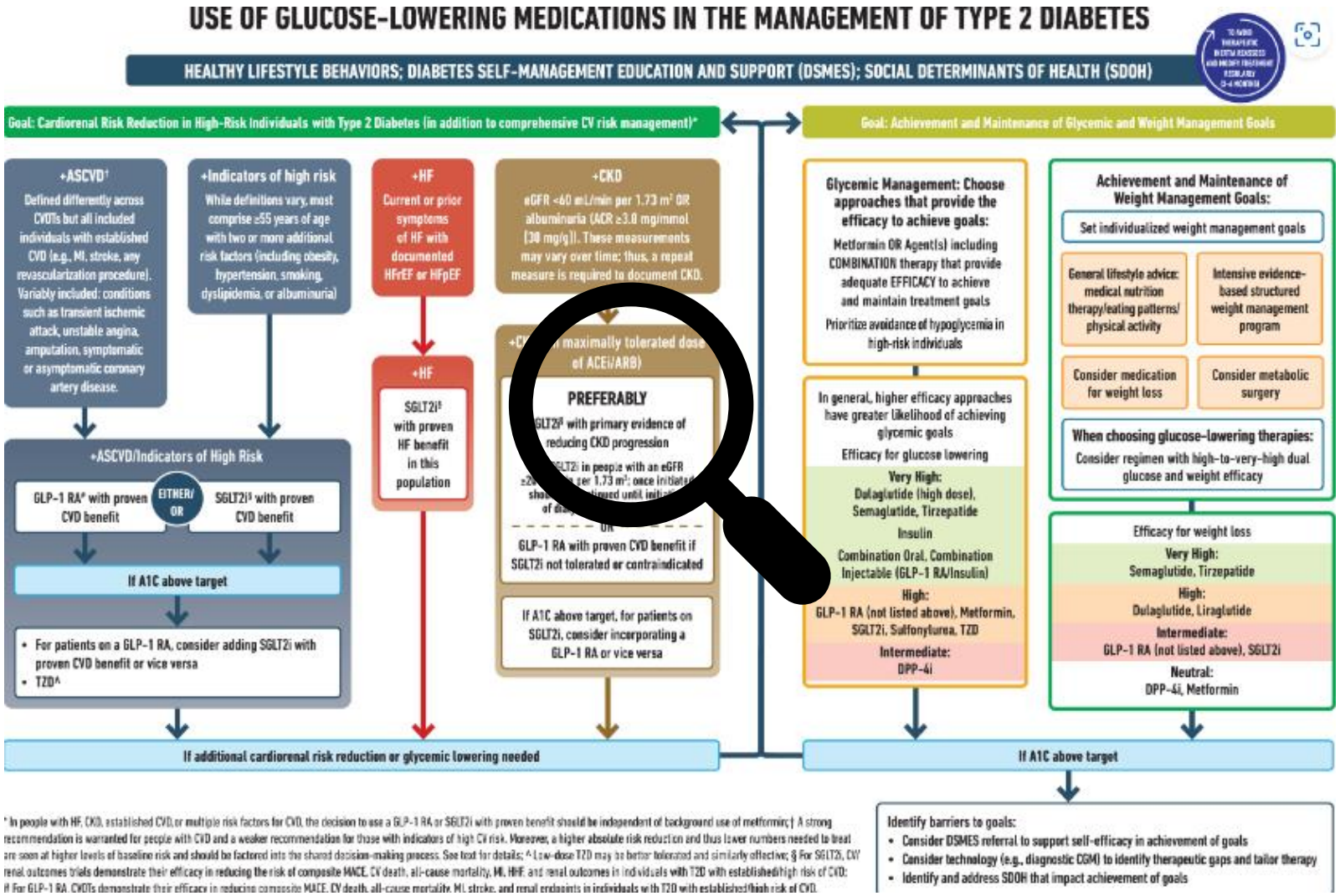
SGLT2i + GLP1a: place in therapy



Without DM

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314.

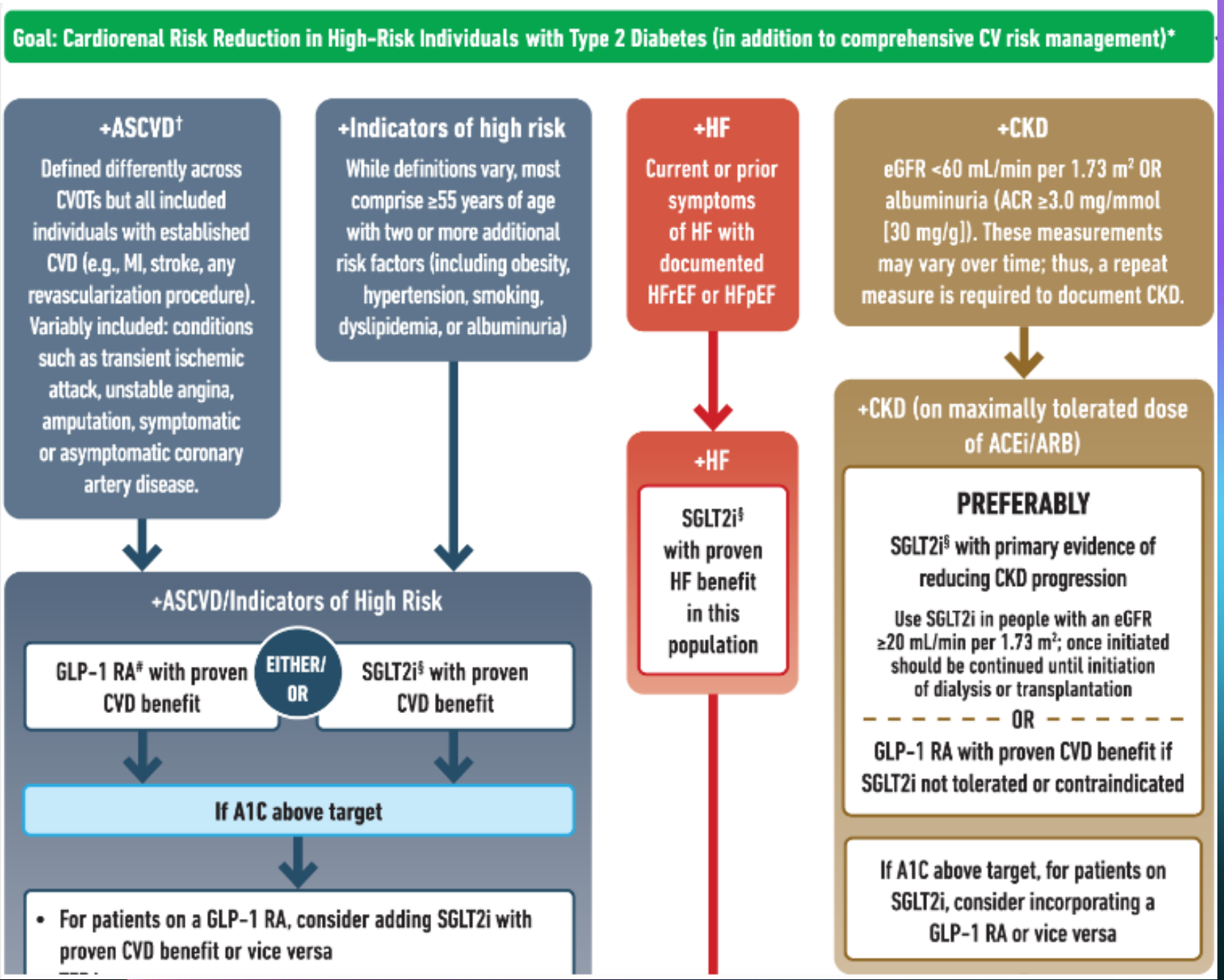
SGLT2i + GLP1a: Place in Therapy



American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

ADA 2024 Summary:

- First decide using shared-decision making with patient if focus is cardiorenal risk or weight management
- Use flowchart to decide if SGLT2i or GLP1a should be added first
- *Note*: metformin is not always first line agent



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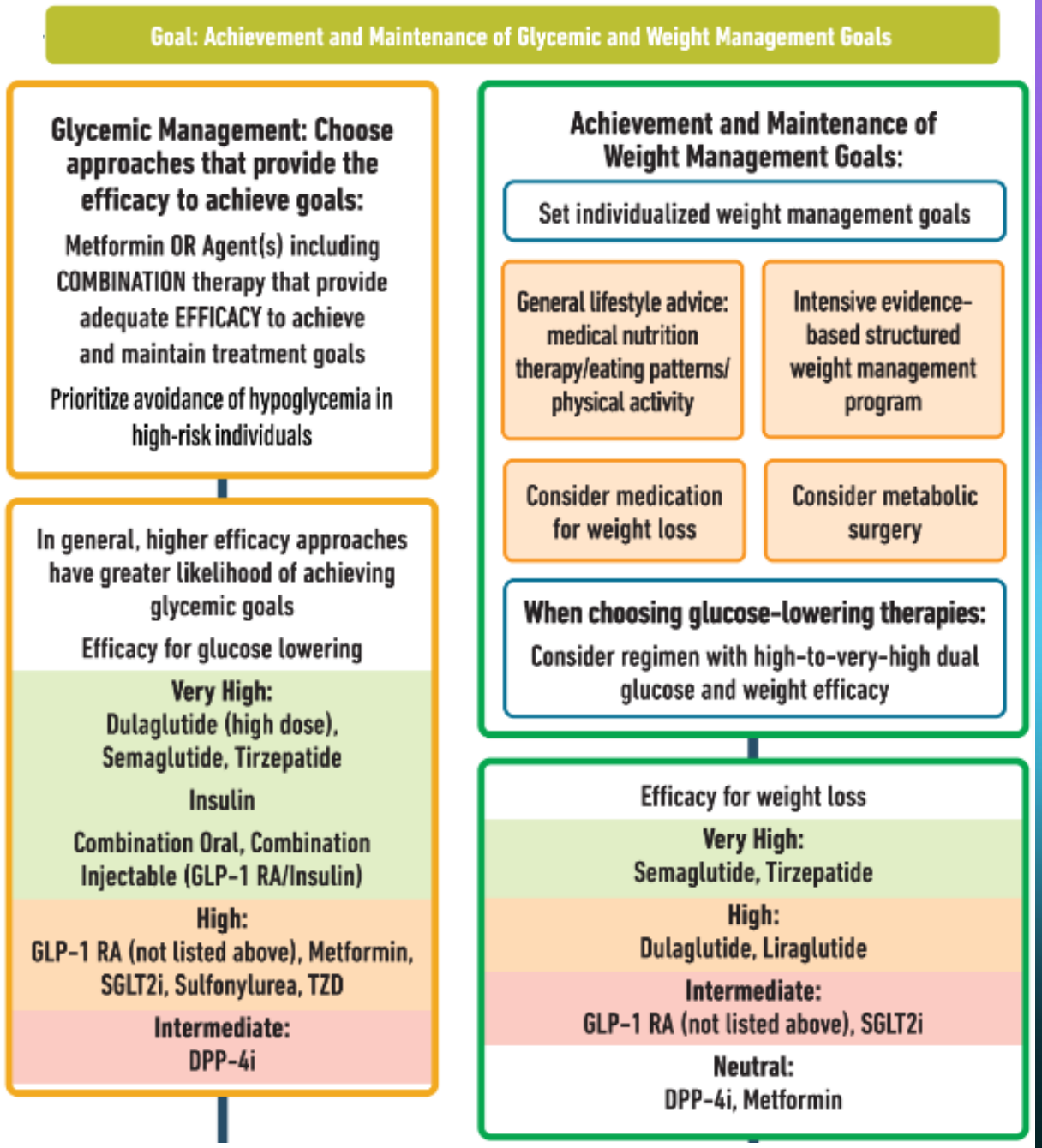


American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

SGLT2i + GLP1a: Place in Therapy

PAD

2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2024;83(24):2497-2604.

- In patients with PAD + T2DM, use of GLP1 and SGLT-2 inhibitors are effective to reduce the risk of MACE (Class 1a).

HF

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. *J Card Fail*. 2022;28(5):e1-e167.
2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2023;81(18):1835-1878.

- HFrEF: SGLT2i (Class 1a)
- HFmrEF: SGLT2i (Class 2a)
- HFpEF: 1st line: SGLT2i (Class 2a); GLP1a add on

CCD (CAD)

2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023;148(9):e9-e119.

- In patients with CAD + T2DM, recommend SGLT2i or GLP1a to reduce risk of MACE (Class 1a)
- In patients with CAD + overweight/obesity GLP1a (semaglutide > liraglutide) is recommended (Class 2a).
- In patients with CAD + HFrEF, an SGLT2i reduces CV death (Class 1a)

SGLT2i + GLP1a: Place in Therapy

Primary CAD Prevention

- It may be reasonable to add a SGLT2i OR GLP1a to metformin in DM with other ASCVD risk factors (Class IIb).

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596-e646.

Atrial Fibrillation

- "In patients with T2DM/HF/CKD, SGLT2i appear to prevent new AF…With only limited or inconsistent data, no recommendations are made for these upstream therapies for prevention of AF"
- No mention of GLP1a

2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149(1):e1-e156.

SGLT2 Inhibitors

Generic Name	Brand Name	Year Approved	Doses Available
Canagliflozin	Invokana®	2013	100mg, 300mg
Dapagliflozin	Farxiga®	2014	5mg, 10mg
Empagliflozin	Jardiance®	2014	10mg, 25mg
Ertugliflozin	Steglatro®	2017	5mg, 15mg
Bexagliflozin	Brenzavvy®	2023	20mg
Sotagliflozin*	Inpefa®	2023	200mg, 400mg

Invokana (canagliflozin). Prescribing Information. Janssen; 2023; Farxiga (dapagliflozin). Prescribing Information. AstraZeneca; 2024; Jardiance (empagliflozin). Prescribing Information. Boehringer Ingelheim; 2023; Steglatro (ertugliflozin). Prescribing Information. Merck; 2023; Brenzavvy (bexagliflozin). Prescribing Information. TheracosBio; 2023; Inpefa (sotagliflozin). Prescribing Information. Lexicon Pharmaceuticals; 2023.

FDA Approved Indications

Generic Name	Diabetes	Heart Failure	CKD
Canagliflozin	✓		
Dapagliflozin	✓	✓	✓
Empagliflozin	✓	✓	✓
Ertugliflozin	✓		
Bexagliflozin	✓		
Sotagliflozin*	✓	✓	✓

Invokana (canagliflozin). Prescribing Information. Janssen; 2023; Farxiga (dapagliflozin). Prescribing Information. AstraZeneca; 2024; Jardiance (empagliflozin). Prescribing Information. Boehringer Ingelheim; 2023; Steglatro (ertugliflozin). Prescribing Information. Merck; 2023; Brenzavvy (bexagliflozin). Prescribing Information. TheracosBio; 2023; Inpefa (sotagliflozin). Prescribing Information. Lexicon Pharmaceuticals; 2023.

GLP-1 Agonists

Generic Name	Brand Name	Year Approved	Pen Type
Semaglutide	Ozempic®, Wegovy®, Rybelsus® - oral	2017, 2021, 2019	Multi-dose, Single-dose, Oral tablet
Dulaglutide	Trulicity®	2014	Single-dose pen
Lixisenatide	Adlyxin®	2016	Single-dose pen
Exenatide	Byetta®, Bydureon® - XR	2005, 2012	Multi-dose, Single dose
Tirzepatide*	Mounjaro®, Zepbound®	2022, 2023	Single-dose
Liraglutide	Saxenda®, Victoza®	2014, 2010	Multi-dose

Wegovy, Ozempic, Rybelsus (Semaglutide). Prescribing Information. Novo Nordisk; 2023; Trulicity (dulaglutide).. Prescribing Information. Eli Lilly; 2023; Adlyxin (Lixisenatide). Prescribing Information. Sanofi; 2023; Byetta, (Exenatide). Prescribing Information. Eli Lilly; 2020. Bydureon (Exenatide). Prescribing Information. AstraZeneca; 2023; Mounjaro, Zepbound (Tirzepatide). Prescribing Information. Eli Lilly; 2023. Victoza, Saxenda (liraglutide). Prescribing Information. Novo Nordisk; 2023.

FDA Approved Indications

Generic Name	Diabetes	Obesity	CVD Risk in DM
Semaglutide	✓ Ozempic®, Rybelsus®	✓ Wegovy®	
Dulaglutide	✓		✓
Lixisenatide	✓		
Exenatide	✓ Byetta®, Bydureon®		
Tirzepatide*	✓ Mounjaro®	✓ Zepbound®	
Liraglutide	✓ Victoza®	✓ Saxenda®	✓ Victoza®

Wegovy, Ozempic, Rybelsus (Semaglutide). Prescribing Information. Novo Nordisk; 2023; Trulicity (dulaglutide).. Prescribing Information. Eli Lilly; 2023; Adlyxin (Lixisenatide). Prescribing Information. Sanofi; 2023; Byetta, (Exenatide). Prescribing Information. Eli Lilly; 2020. Bydureon (Exenatide). Prescribing Information. AstraZeneca; 2023; Mounjaro, Zepbound (Tirzepatide). Prescribing Information. Eli Lilly; 2023. Victoza, Saxenda (liraglutide). Prescribing Information. Novo Nordisk; 2023.

Audience Participation

Which of the following the GLP1-agonists is FDA approved to reduce the risk of major CV events in patients with DM?

A. Liraglutide
B. Dulaglutide
C. Tirzepatide
D. A + B
E. All of the above

Audience Participation

Which of the following the GLP1-agonists is FDA approved to reduce the risk of major CV events in patients with DM?

A. Liraglutide
B. Dulaglutide
C. Tirzepatide
D. A + B
E. All of the above

Common SGLT2i ADRs

- Genital mycotic infections
- Urosepsis and pyelonephritis (UTI)
- Lower limb amputation
- Diabetic ketoacidosis (DKA)
- Acute kidney injury
- Hypoglycemia

American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

Common GLP-1a ADRs

- Nausea
- Constipation
- Diarrhea
- Vomiting
- Decreased appetite

American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

Missed Doses / Drug Storages

TABLE 2 Considerations for Resuming a GLP-1 Receptor Agonist After a Prolonged Lapse in Therapy

Agent	Last Dose Administered	Recommendation(s) for Resuming Therapy
Dulaglutide*	1.5 mg once weekly	• Resume at 1.5 mg once-weekly dose. • Expect comparable tolerability to that experienced prior to dose interruption.
	3 or 4.5 mg once weekly	• Use best judgment if ≥3 doses are missed. ○ It is unknown whether tolerance to the GI adverse events will remain if reinitiated at the higher dose after ≥3 missed doses. ○ Decision can be informed by patient's prior GI tolerability. ○ In consideration of the above, clinicians may consider reinitiating at 1.5 mg once weekly.
Injectable semaglutide†	1 mg once weekly	• If ≤2 doses are missed, reinitiate at 1 mg once weekly. • If 3–4 doses are missed, reinitiate at 0.5 mg weekly. • If ≥5 doses are missed, reinitiate at 0.25 mg once weekly.
Tirzepatide‡	≥5 mg once weekly	• If ≤2 doses are missed, reinitiate at the same dose (provided the dose was adequately tolerated). • If ≥3 doses are missed, reinitiate at 5 mg once weekly.

Whitley HP, Trujillo JM, Neumiller JJ. Special Report: Potential Strategies for Addressing GLP-1 and Dual GLP-1/GIP Receptor Agonist Shortages. *Clin Diabetes*. 2023;41(3):467-473.

TABLE 1 Manufacturer Recommendations for Missed Doses of GLP-1 Receptor Agonists

Agent	Recommended Dosing Interval	Manufacturer Recommendations for Missed Doses
Short-acting agents		
Exenatide	Twice daily	• Skip missed dose and resume at the next scheduled dose.
Lixisenatide	Once daily	• If a dose is missed, administer within 1 hour prior to next meal.
Long-acting agents		
Dulaglutide	Once weekly	• Administer as soon as possible if there are ≥3 days (72 hours) until next scheduled dose. • If <3 days before next scheduled dose, skip the missed dose and administer on the next scheduled day.
Exenatide XR	Once weekly	• Administer as soon as possible if there are ≥3 days (72 hours) until the next scheduled dose. • If <3 days before next scheduled dose, skip the missed dose and administer on the next scheduled day.
Liraglutide	Once daily	• If dose is missed, resume with the next scheduled dose.
Semaglutide (injectable)	Once weekly	• Administer as soon as possible within 5 days after the missed dose. • If >5 days have passed, skip the dose and administer on the next scheduled day.
Semaglutide (oral)	Once daily	• If dose is missed, resume with the next scheduled dose.
Tirzepatide	Once weekly	• Administer as soon as possible within 4 days (96 hours) after the missed dose. • If >4 days have passed, skip the dose and administer on the next scheduled day.

Whitley HP, Trujillo JM, Neumiller JJ. Special Report: Potential Strategies for Addressing GLP-1 and Dual GLP-1/GIP Receptor Agonist Shortages. *Clin Diabetes*. 2023;41(3):467-473.

Important Points

- Chronic condition = long-term medication
- Rotate injection site
- Check stability for each product especially given frequent power outages/hurricanes
- Same medication, different formulations
  - Ex – Wegovy® vs Ozempic® single vs. multi-dose pen

Do not use SGLT2i if…

- Pregnancy
- Breast feeding
- Hypovolemic
- Severe renal impairment or HD
- Type 1 Diabetes
- Hypersensitivity

American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

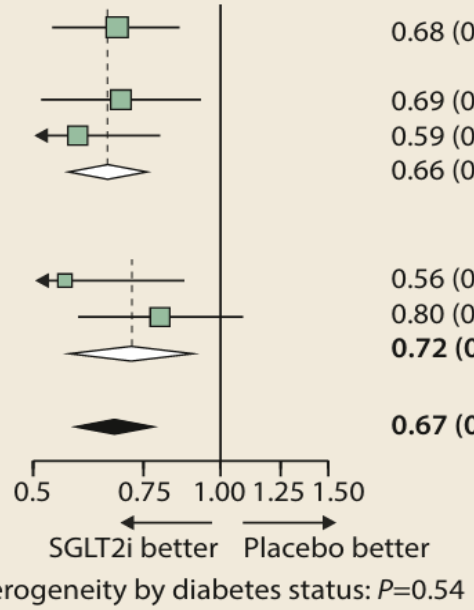
Do not use GLP-1 agonists if…

- Type 1 DM
- Pancreatitis
- Thyroid cancer
- Pregnant
- Severe renal dysfunction

American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S322.

SGLT2i outcomes

	Mean baseline eGFR (ml/min/1.73 m²)	Events/participants		Rate per 1000 patient-years		Relative risk (95% CI)	Trend across trials sorted by eGFR
		SGLT2i	Placebo	SGLT2i	Placebo		
Diabetes							
CREDENCE	56	116/2202	165/2199	20	29	0.68 (0.54, 0.86)	
SCORED	44	NA/NA	NA/NA	26	37		
DAPA-CKD	44	77/1455	109/1451	24	39	0.69 (0.51, 0.92)	*P*=0.48
EMPA-KIDNEY	36	74/1525	116/1515			0.59 (0.44, 0.79)	
Subtotal: DIABETES	**47**	**267/5182**	**390/5165**			0.66 (0.56, 0.77)	
No diabetes							
DAPA-CKD	42	32/697	52/701	24	39	0.56 (0.36, 0.87)	*P*=0.19
EMPA-KIDNEY	39	83/1779	105/1790	25	31	0.80 (0.60, 1.07)	
Subtotal: NO DIABETES	**40**	**115/2476**	**157/2491**			**0.72 (0.56, 0.91)**	
TOTAL: OVERALL	**45**	**382/7658**	**547/7656**			**0.67 (0.59, 0.77)**	



Heterogeneity by diabetes status: *P*=0.54

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314.

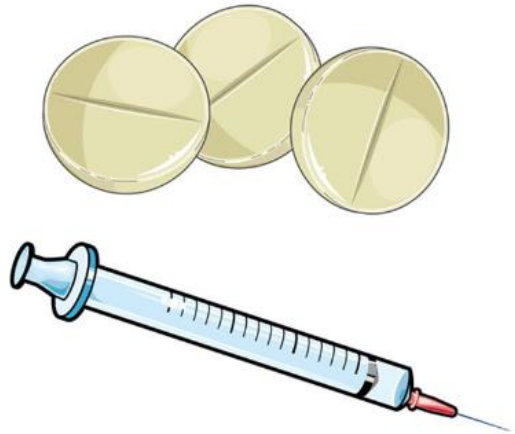
GLP-1 agonist outcomes

GLP-1 receptor agonists

Effects on CV outcomes

(HR; 95%CI)

- MACE 0.86 (0.80 to 0.93)
- MI 0.90 (0.83 to 0.98)
- Stroke 0.83 (0.76 to 0.92)
- CV death 0.87 (0.80 to 0.94)



Effects on risk factors

glucose | weight | blood pressure

HbA1 ~ 1.5 % | **~ 4%** | **~ 3 mmHg**

Side effects

- GI side effect
- Local reaction at injection side
- Use with caution in patients with history of pancreatitis

Patient profile

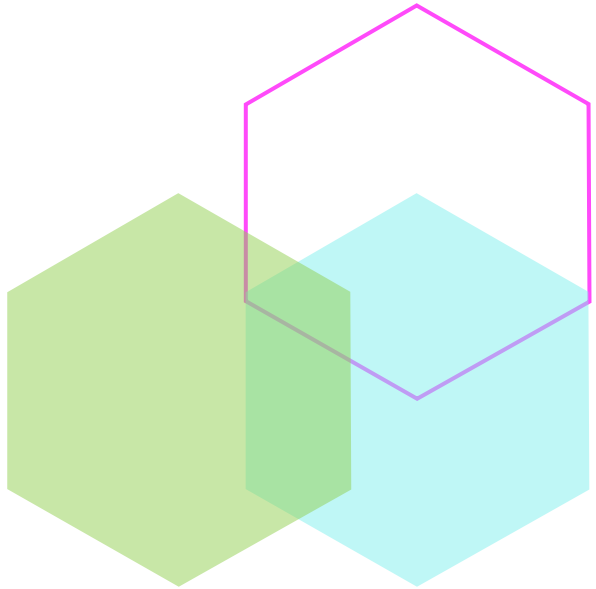
- ASCVD
- Overweight / obese
- High risk of stroke

Treatments aspects

- Start with low dose
- Increase dose slowly
- Use ≤ 32 gauge needle
- Adjust insulin / SU dose
- Recommend small meals

Marx N, Husain M, Lehrke M, Verma S, Sattar N. GLP-1 Receptor Agonists for the Reduction of Atherosclerotic Cardiovascular Risk in Patients With Type 2 Diabetes. *Circulation*. 2022;146(24):1882-1894.

Group Activity



Instructions:

1. Break into small groups
2. Review the case provided to your group
3. Answer the questions included with your case
4. Choose someone in the group to share/present to the larger group

Pharmacist’s Role

- Patient education, patient education, patient education!
- Recognize social determinants of health
- The link between multiple providers, working in silos, not communicating
- Role of primary care in early identification and prevention
- Deprescribing when appropriate
- Expanding role as providers

Post-Test

1. Guidelines are shifting from treatment of diabetes as the only condition to reduction of overall cardio-renal-metabolic comorbidities. True False
2. To reduce overall mortality in patients with T2D, sitagliptin is preferred in those with HF or CKD. True False
3. In patients with high risk of ASCVD or with established CVD, GLP-1RAs and SGLT2is are preferred agents. True False
4. Clinical pharmacists can help identify patients with diabetes who may benefit from GLP-1 RAs or SGLT2is to optimize their glycemic control and provide positive cardiorenal benefits. True False
5. Pharmacists can educate team members on the benefits and risks of SGLT2 inhibitors or GLP-1RA beyond glycemic control. True False

Educación Continua

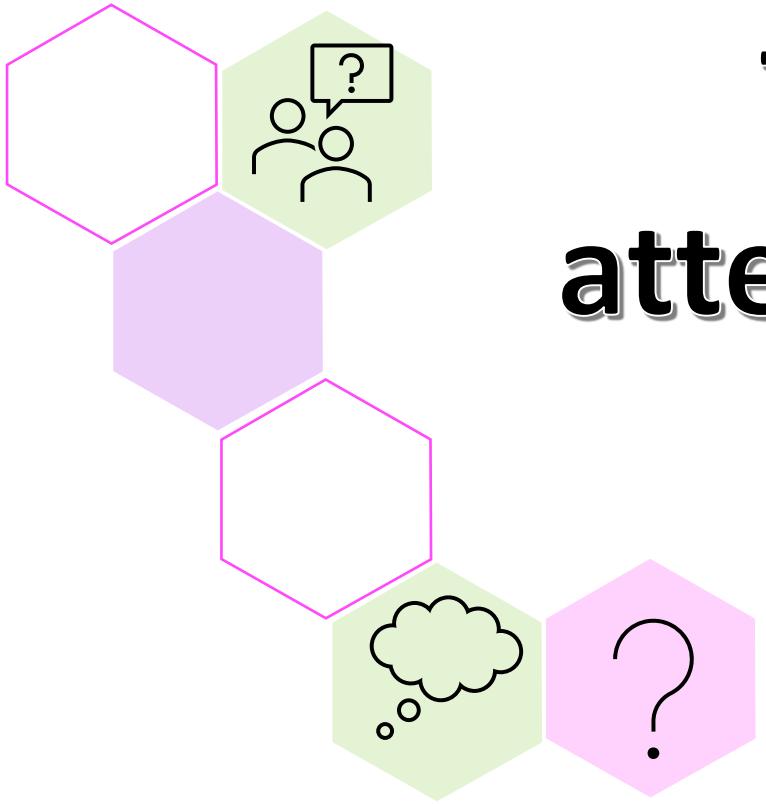
1. Log in en tu cuenta de **CFPR.org**
2. Click en **MI CUENTA**
3. Click en **HISTORIAL DE CURSOS**
4. Seleccionar el curso
5. Completar la evaluación y Prueba
6. Guardar o imprimir el Certificado

Access Code

CPE MONITOR

CODE

Tiene hasta el 5 de Octubre para completar la evaluación y prueba y poder obtener su certificado



Thank you for your attention & participation!

Questions?

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