MAYO CLINIC

INTEGRATING RISK FACTORS AND HEALTHY LIFESTYLE APPROACHES

Amy West Pollak, MD MSc FAHA
Chair, Division of Cardiac Subspecialities
Co-Director, Women's Heart Clinic
Mayo Clinic, Florida

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Health Equity Advisory Council for Janssen (unpaid)

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

“Let food be thy medicine and let thy medicine be food.”

Hippocrates 440 BCE

LEARNING OBJECTIVES

- Understand the complex factors that lead to obesity
- Compare dietary approaches to reduce cardiovascular events
- Explore the relationship between dietary approaches and longevity

OUTLINE
INTEGRATING RISK FACTORS AND HEALTHY LIFESTYLE APPROACHES

- Individualize cardiovascular risk
- Weight management isn’t just calories in < calories out
- Dietary approaches for reduction in cardiovascular risk
- Overall approach for heart health
- When lifestyle alone isn’t enough and meds are needed

1 INDIVIDUALIZE CV RISK

CASE:
65 YEAR OLD WOMAN WITH FAMILY HX OF CAD

- 65 yo post-menopausal woman presents for a cardiovascular wellness evaluation given that her brother had a MI at age 54.
  - 30 pack year history of tobacco use, now just occasional
  - Follows a Mediterranean diet
  - Walking limited by exertional leg fatigue after 2 blocks

CASE:
65 YEAR OLD WOMAN WITH FAMILY HX OF CAD

- **Physical Exam**:
  - BP 107/71 and BMI 32 mg/k2
  - Decreased pedal pulses
- **Labs**:
  - LDL 135 mg/dl, HDL 32 mg/dl, TG 75 mg/dl
  - Pre-diabetes with A1c 6.2%, eGFR 75
  - ASCVD 10-year risk: 3%
  - EKG normal with heart rate 58 bpm

PREVENT™ Online Calculator

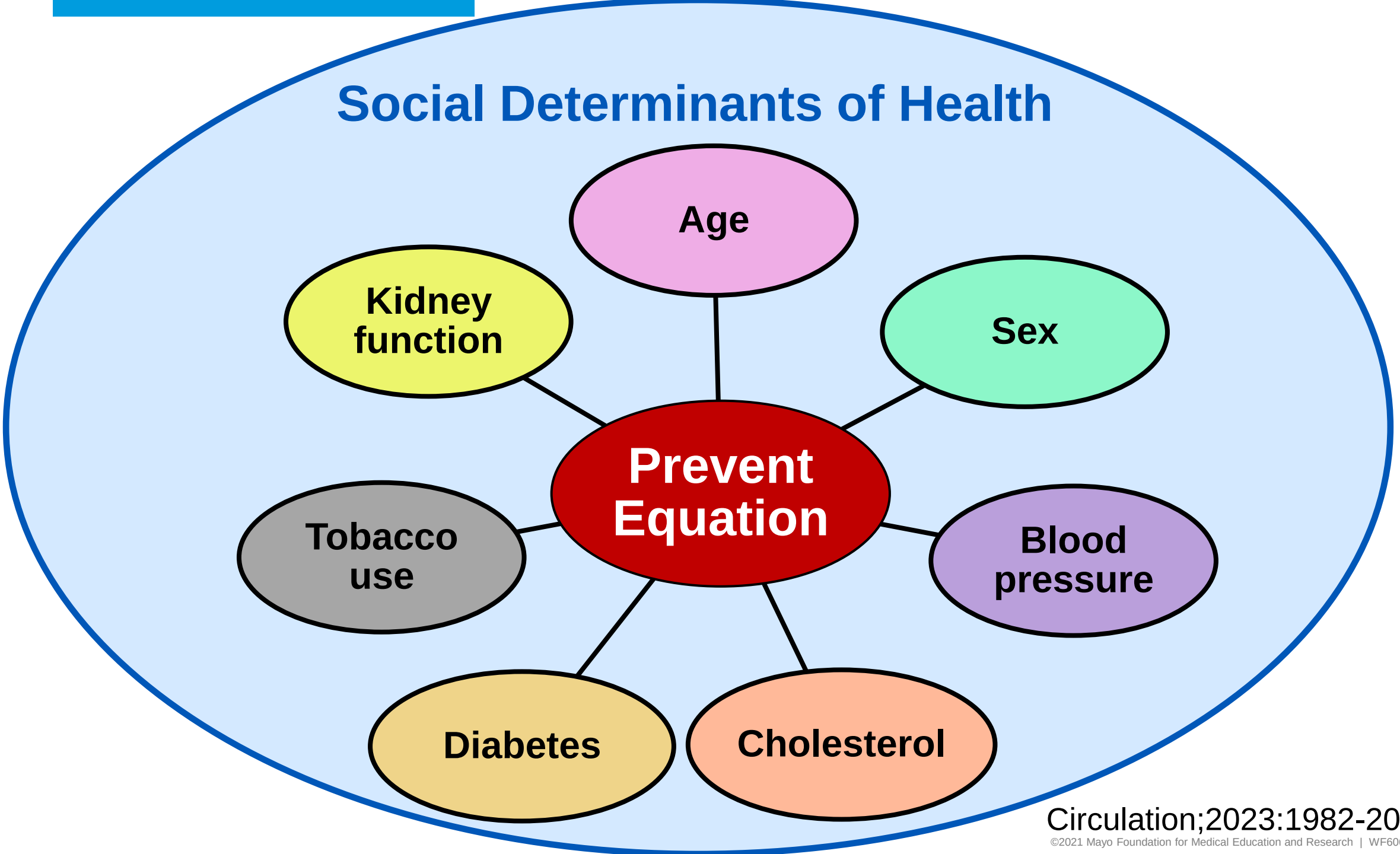
Welcome to the American Heart Association **Predicting Risk of cardiovascular disease EVENTs** (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

PREVENT RISK CALCULATOR: DIFFERENCES FROM ASCVD RISK SCORE

- Integrates Cardiovascular-kidney-metabolic syndrome (includes eGFR)
- Includes risk for heart failure as well as ASCVD
- 10-year and 30-year risk for individuals between 30-79 years
- Integrates Social Deprivation Index
- Calibrated across broad sociodemographic subgroups
- Sex-specific but race free

Circulation;2023:1982-2004

Social Determinants of Health



Circulation;2023:1982-2004

QUESTION:
WHAT DO YOU RECOMMEND AS A NEXT STEP?

A. Start statin therapy

B. Recommend increasing exercise and weight loss alone

C. Check lipoprotein (a) to guide LDL goal

D. Coronary CTA given limited walking ability (2 blocks)

E. ABI testing

F. D and E

WHAT ARE SOME RISK-ENHANCING FACTORS FOR MANAGEMENT OF CHOLESTEROL?

Premature ASCVD

M < 55 yo

F < 65 yo

LDL-C

160-189 mg/dl

Metabolic Syndrome

CKD

(eGFR 15-59 ml/min/1.73m2)

Chronic inflammatory conditions

Premature menopause & Pre-eclampsia

hsCRP > 2 mg/dl

Lp (a) > 50 mg/dl

Apolipo B > 130 mg/dl

ABI < 0.9

Circulation.2019;11:e563-e595

SEX-SPECIFIC RISK FACTORS FOR CVD

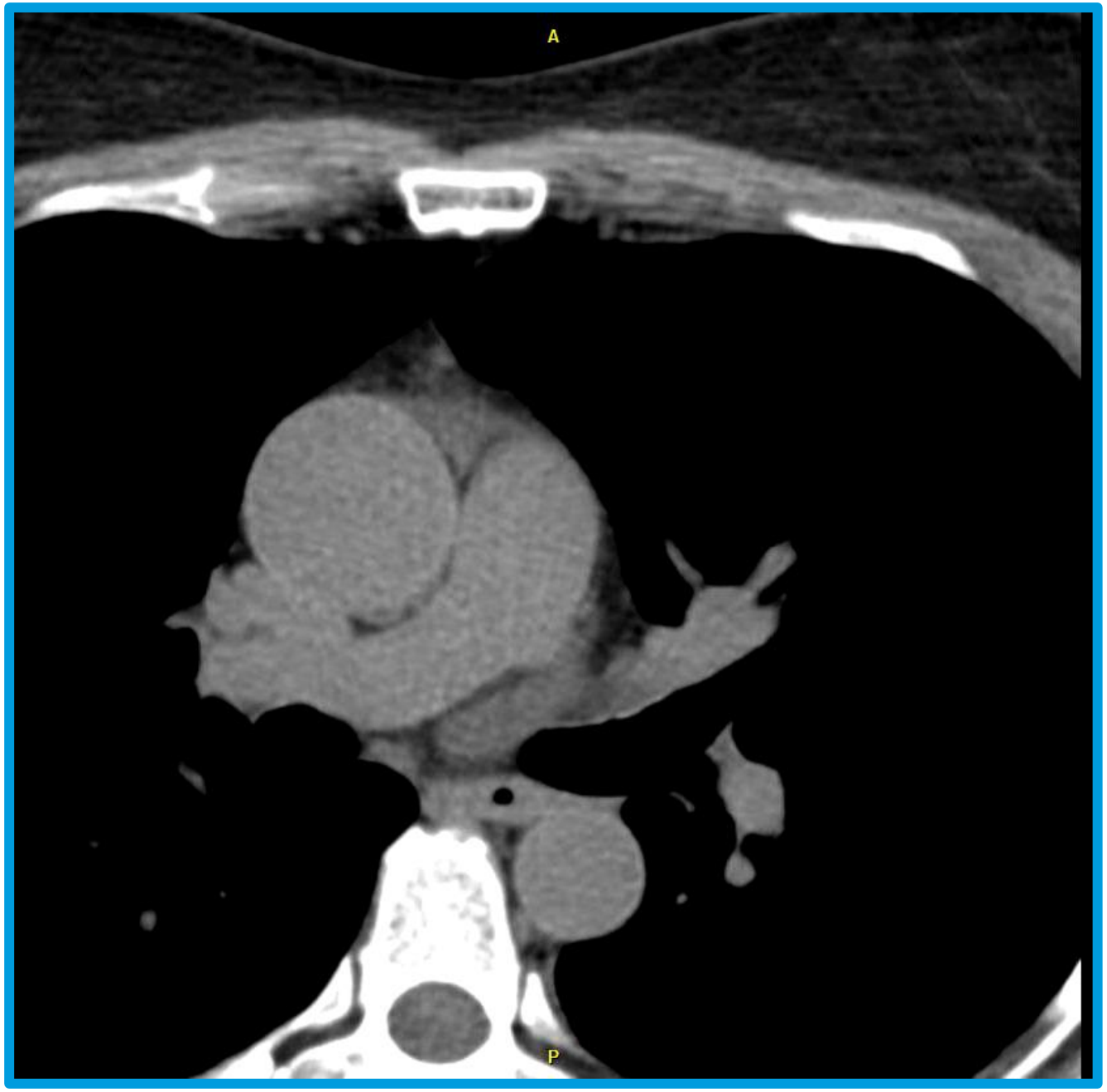
- **Pregnancy-related factors** (preeclampsia, gestational diabetes or hypertension, miscarriages, preterm delivery)
- **Menstrual cycle history** (age at start of menarche and menopause)
- **Hormone medications** (contraception, hormone therapy)
- **Polycystic ovarian syndrome**
- **Autoimmune disorders**
- **Chemotherapy or radiation therapy** for breast cancer

Mehta et al. Circulation 2023;147:1471-1487

HEALTH DISPARITIES

Race and ethnicity → social, cultural, environmental, systemic, and demographic constructs

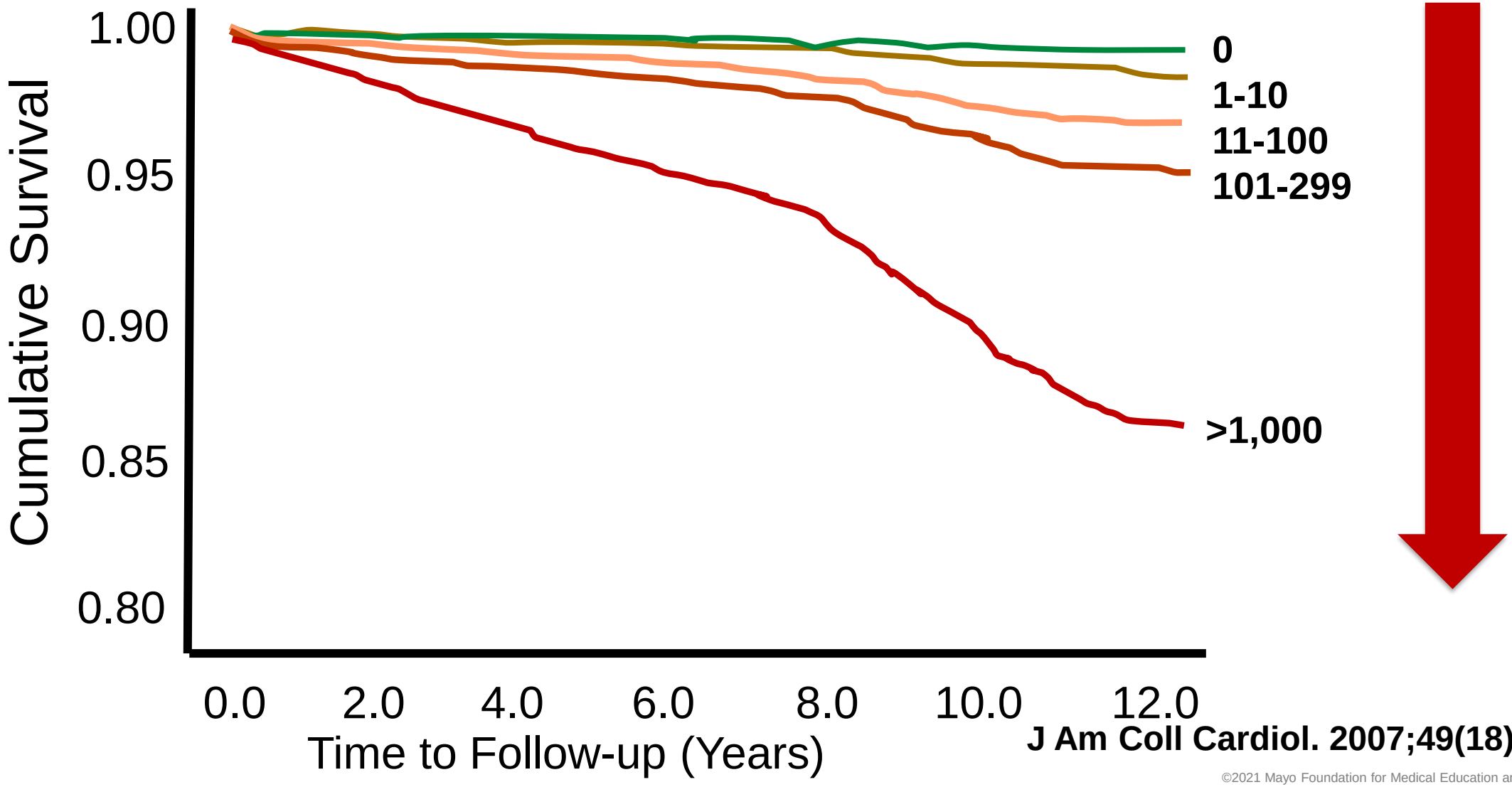
Mehta et al. Circulation 2023;147:1471-1487



Calcium Score:
1257

CORONARY CALCIUM:

↑CACS = ↓Survival



J Am Coll Cardiol. 2007;49(18)1860-1870

PATIENT CASE

- Her ABI’s are abnormal at 0.85 right and 0.79 on the left
- Lipoprotein a is elevated at 175 nmol/L (uln 75 nmol/L)

WHAT DO YOU RECOMMEND FOR HER LDL CHOLESTEROL GOAL?

A. < 100 mg/dl

B. < 70 mg/dl

C. < 55 mg/dl

D. As low as you can go

VERY HIGH RISK FOR FUTURE ASCVD EVENTS

Major ASCVD Events	High-Risk Conditions
ACS within last 12 months	≥ 65 years old
Myocardial infarction	Familial hyperlipidemia
Ischemic stroke	CABG or PCI
Symptomatic PAD	Diabetes
Amputation or prior revasc	HTN
	CKD eGFR < 60 ml/min/1.73m2
	Tobacco use current
	LDL > 100 on max statin + ezetimibe
	CHF

Very High Risk =

❑ 2 Major ASCVD

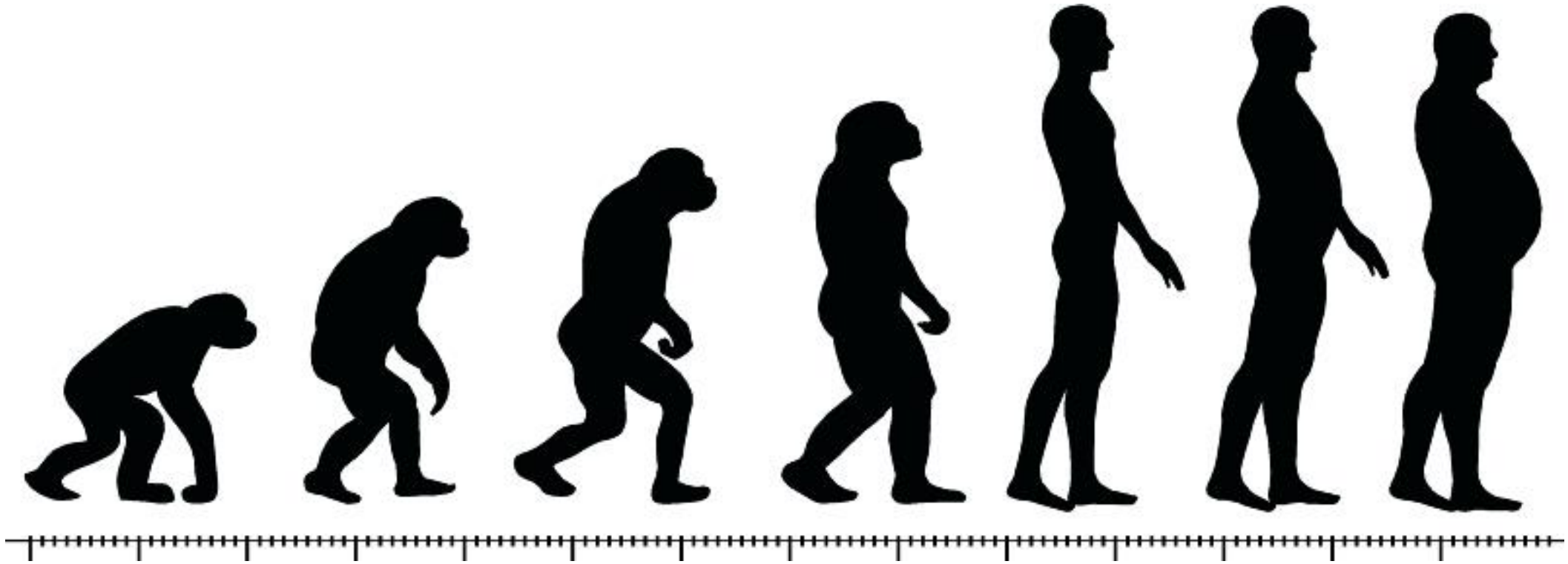
❑ 1 Major + 2 High-Risk Conditions

Circulation.2019;11:e563-e595

TAKE HOME PEARLS #1

- XX

2 WEIGHT MANAGEMENT ISN'T JUST CALORIES IN < CALORIES OUT



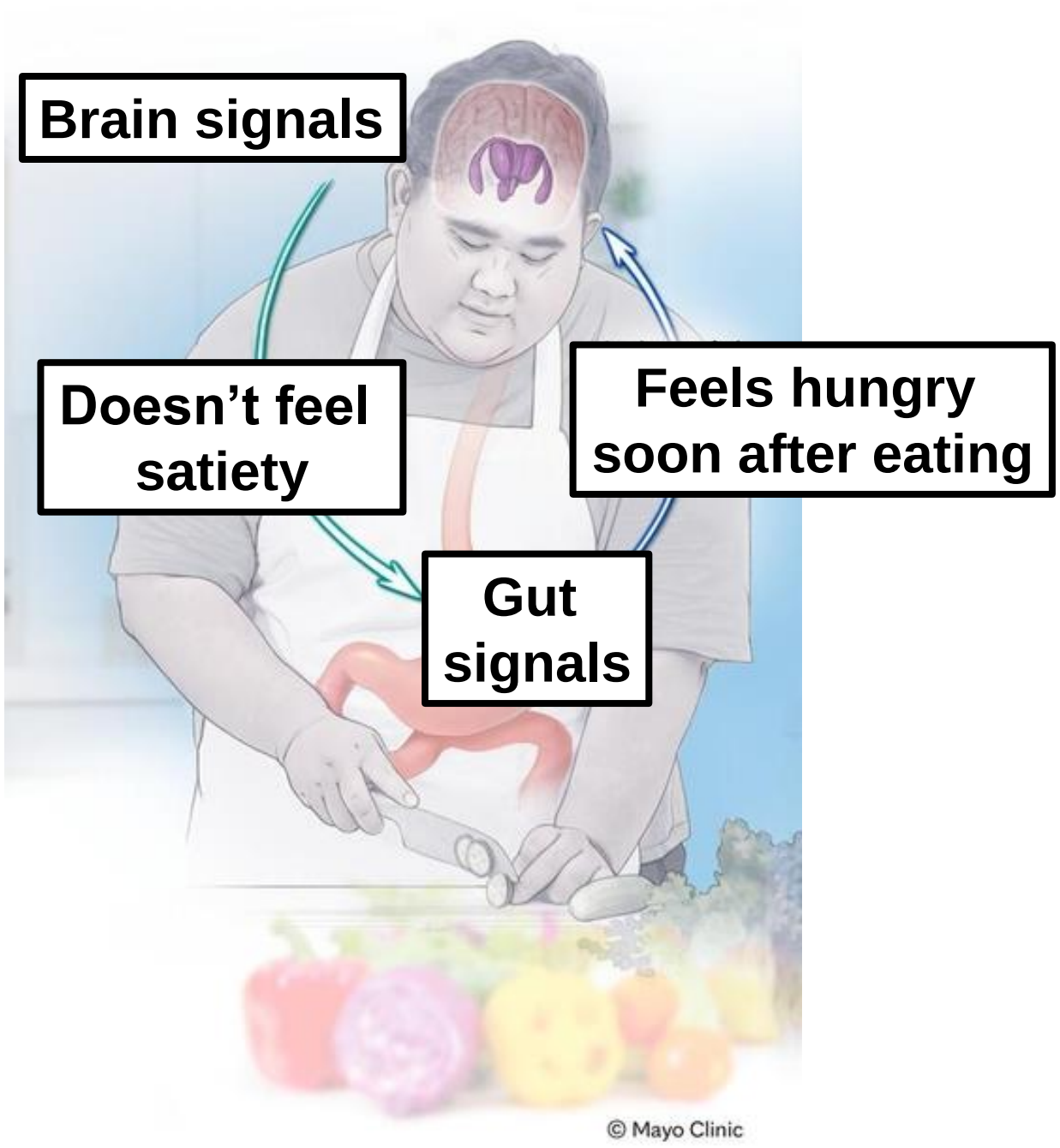
Since 1970 daily calorie intake in the US increased by 20% (425 Kcal/day)

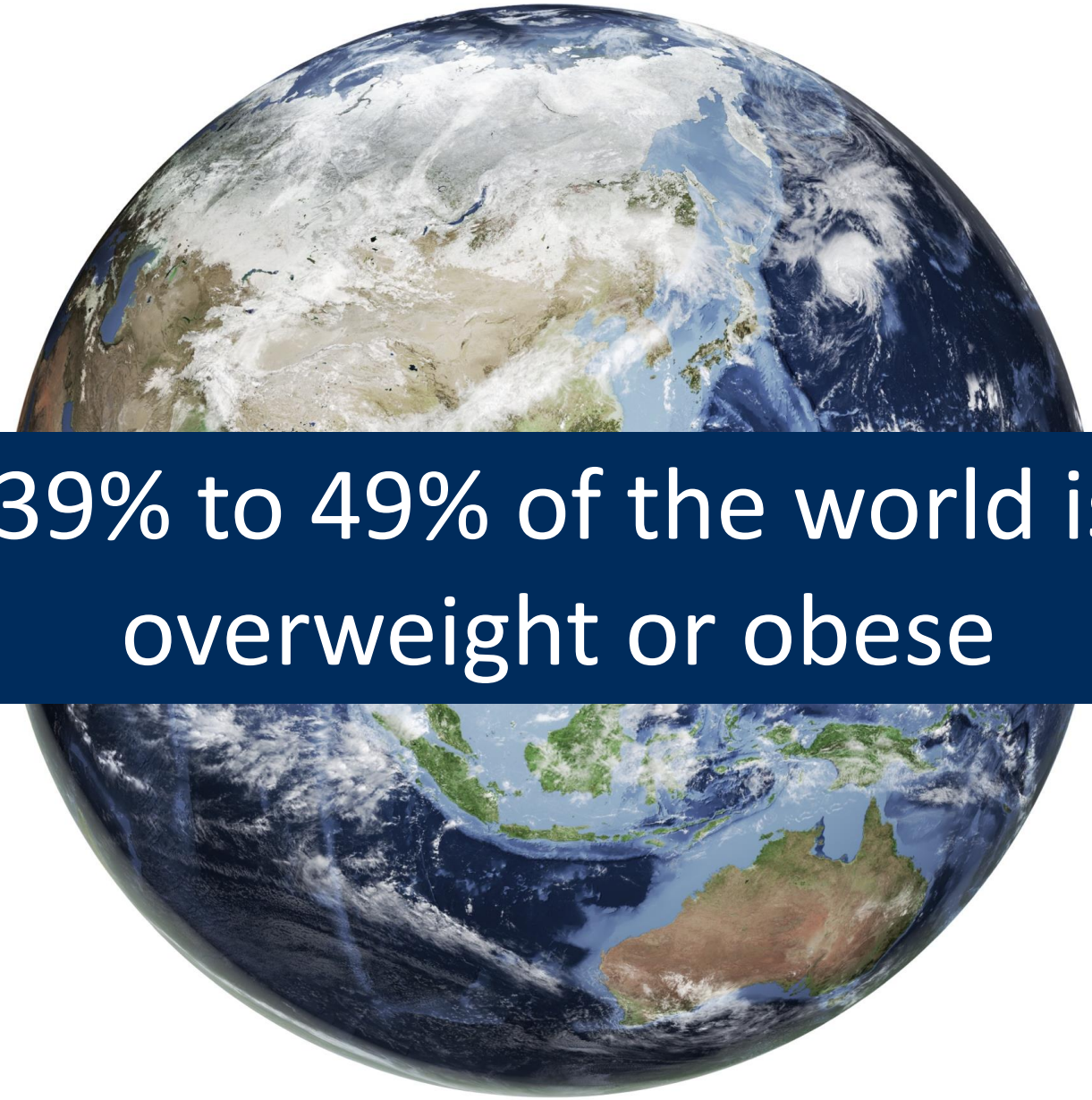
WHY DO WE MAKE LESS-HEALTHY FOOD CHOICES?

Fatigue	**Pleasure**	**Cost**
Stress	**Reward**	**Time**
Lack of Confidence	**Social Pressure**	**Insurmountable**

High sugar, starch, saturated fat and protein

Insulin resistance, hyperglycemia, high IGF-1, high cholesterol





39% to 49% of the world is overweight or obese

PATIENTS WITH OBESITY:
INCREASED CV RISK (PRIMARY PREVENTION)

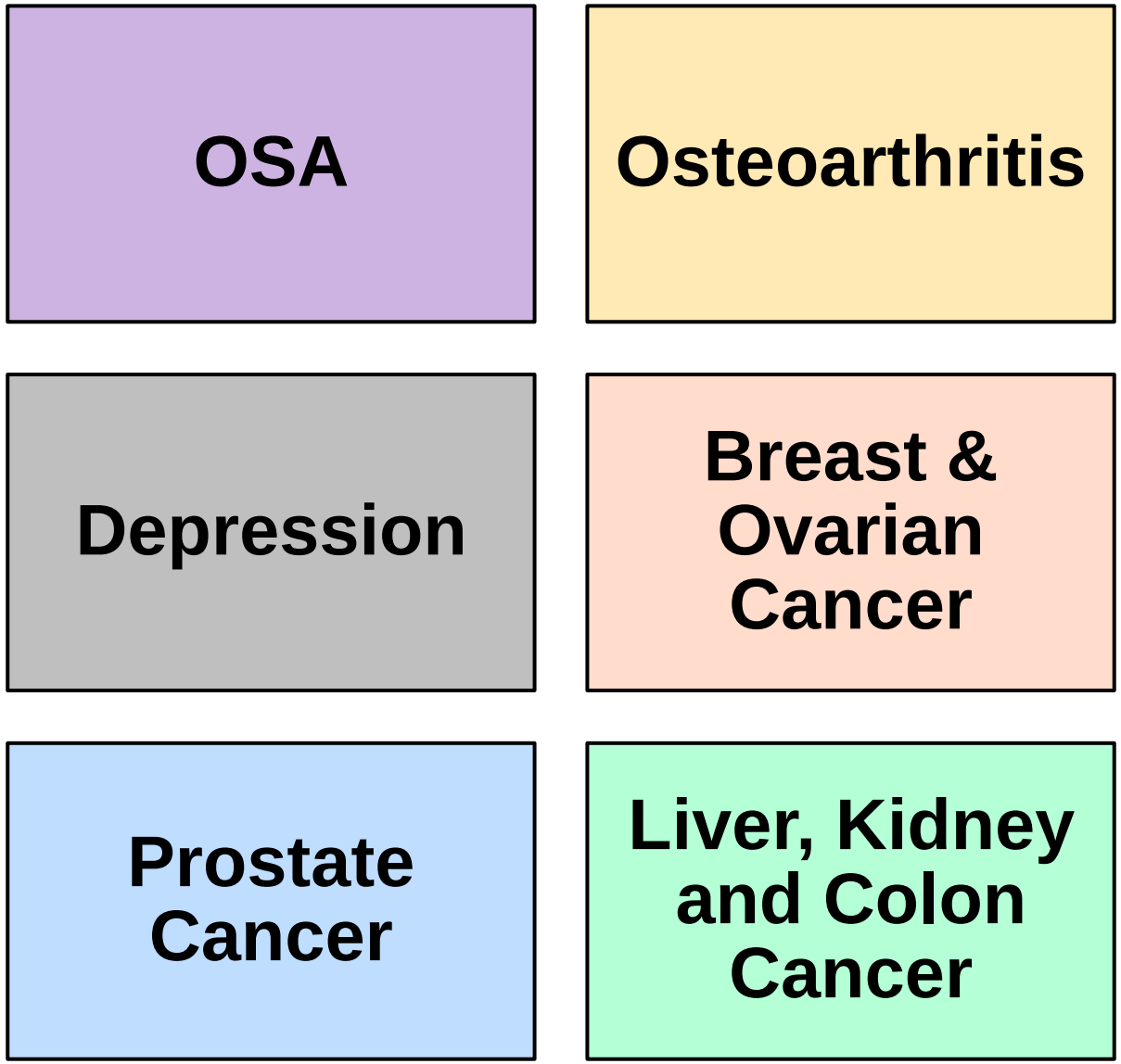
CVD events earlier age

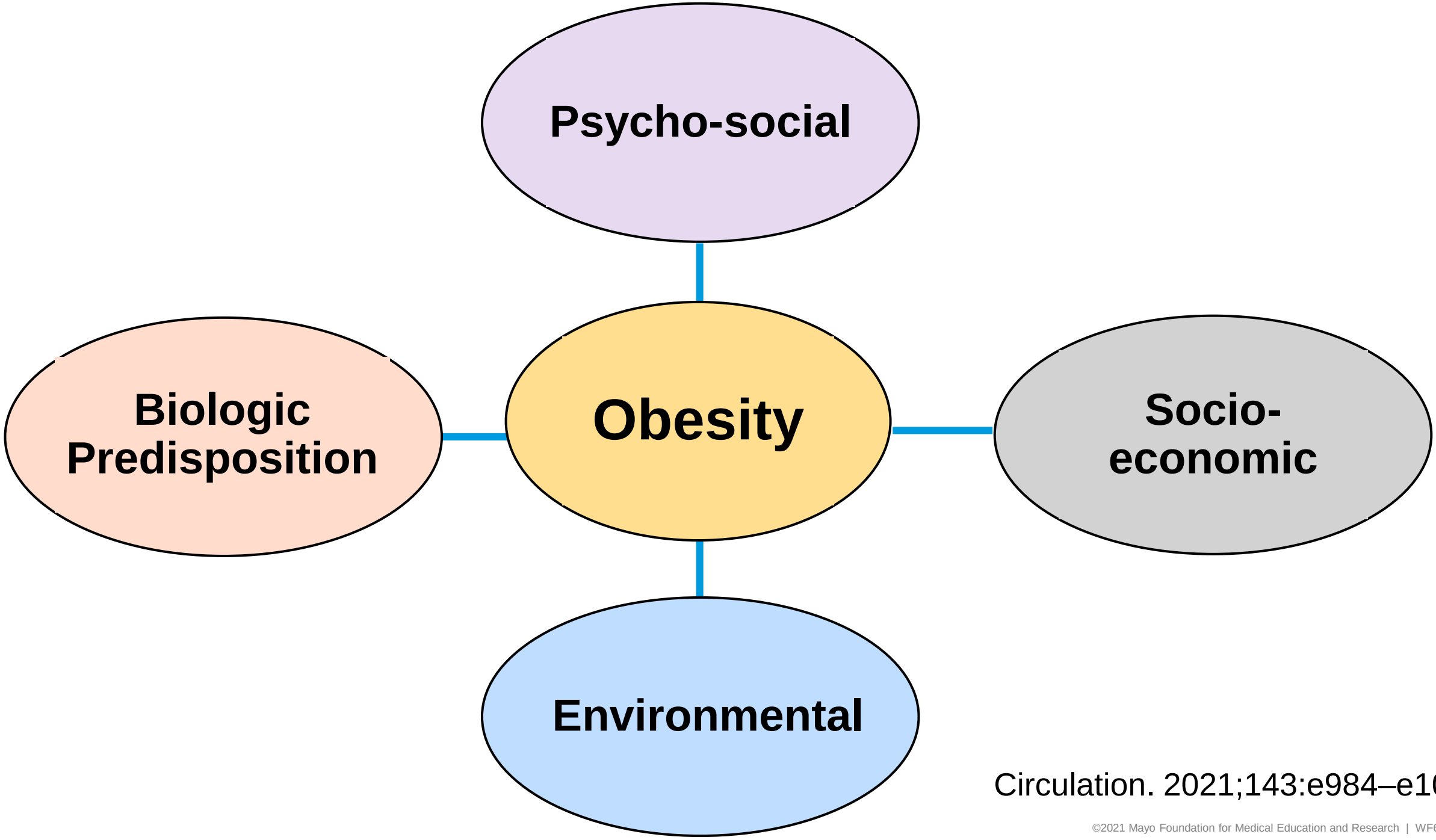
Live with CVD longer

Shorter than avg life span

JAMA Cardiol. 2018;3:280–287

INCREASED RISK WITH OBESITY





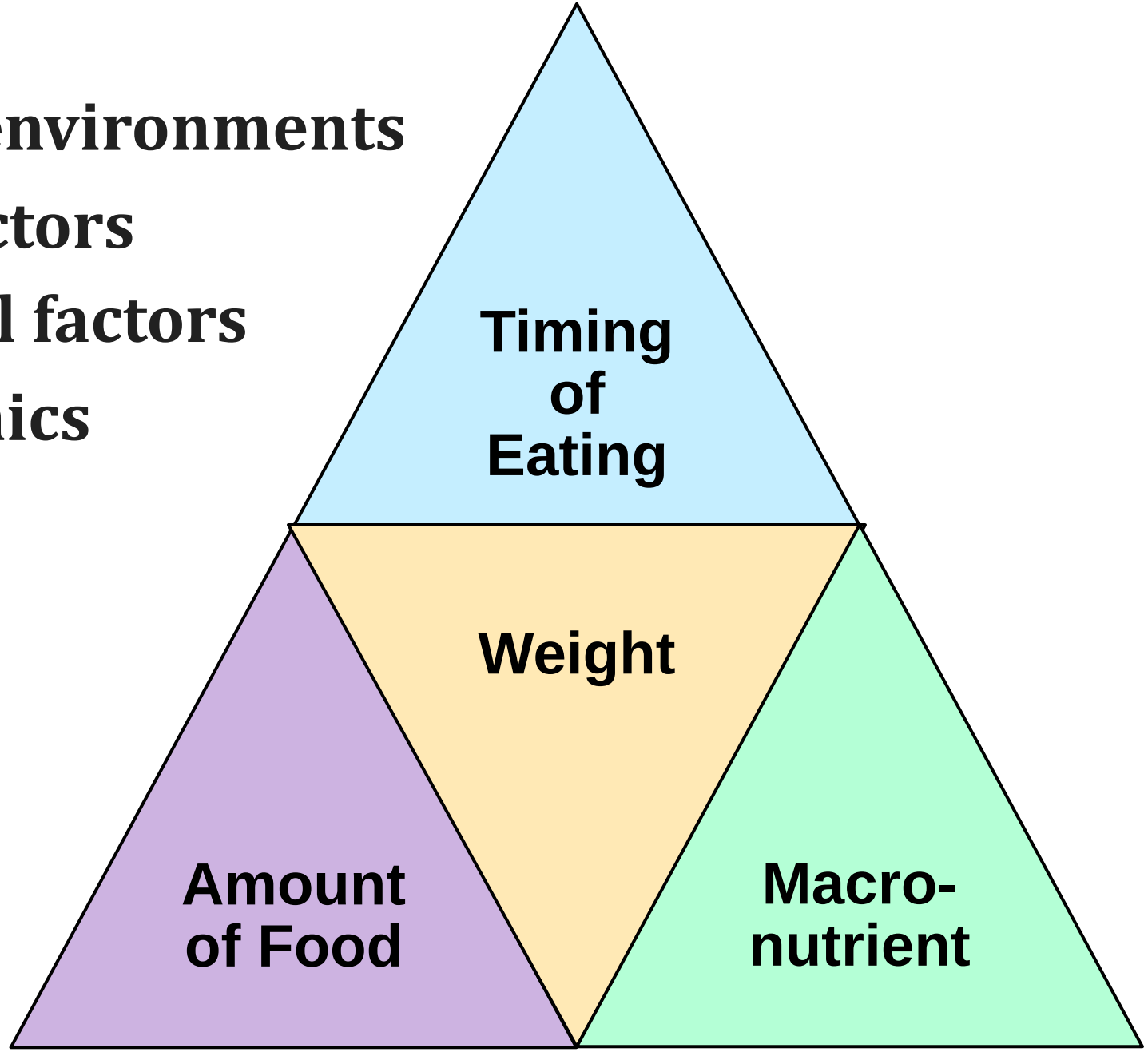
Circulation. 2021;143:e984–e1010

Obesogenic environments

Biological factors

Psychological factors

Socioeconomics



Energy Deficit = Weight Loss

Eat Less and Move More?

PATIENT CASE

- 68 year old woman with a history of type 2 diabetes, hypertension, hyperlipidemia and obesity (**BMI 39 mg/kg2**)

  - **Medications:**
    - Metformin 1000mg bid,
    - Lisinopril 20mg daily, HCTZ 25mg daily
    - Rosuvastatin 20mg daily

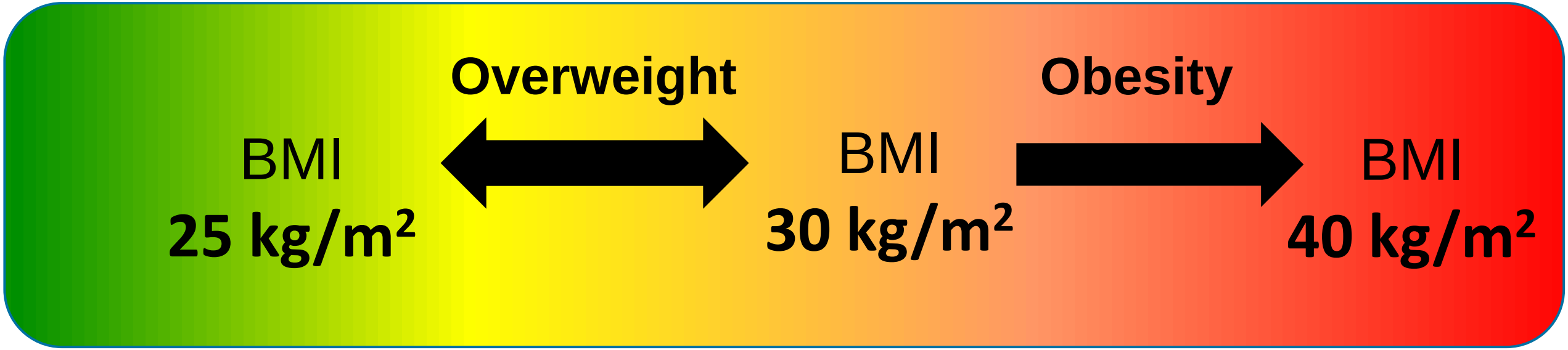
  - **Labs:**
    - A1c 7.8%
    - Cholesterol (mg/dl): Total 225, HDL 39, TG 212 and LDL 98

QUESTION

- What dietary approach do you recommend for weight loss and improvement in metabolic parameters?

A. Ketogenic diet
B. Mediterranean diet
C. Paleo diet
D. Vegetarian or Vegan diet
E. Calorie restriction alone

WORLD HEALTH ORGANIZATION
CRITERIA FOR OBESITY



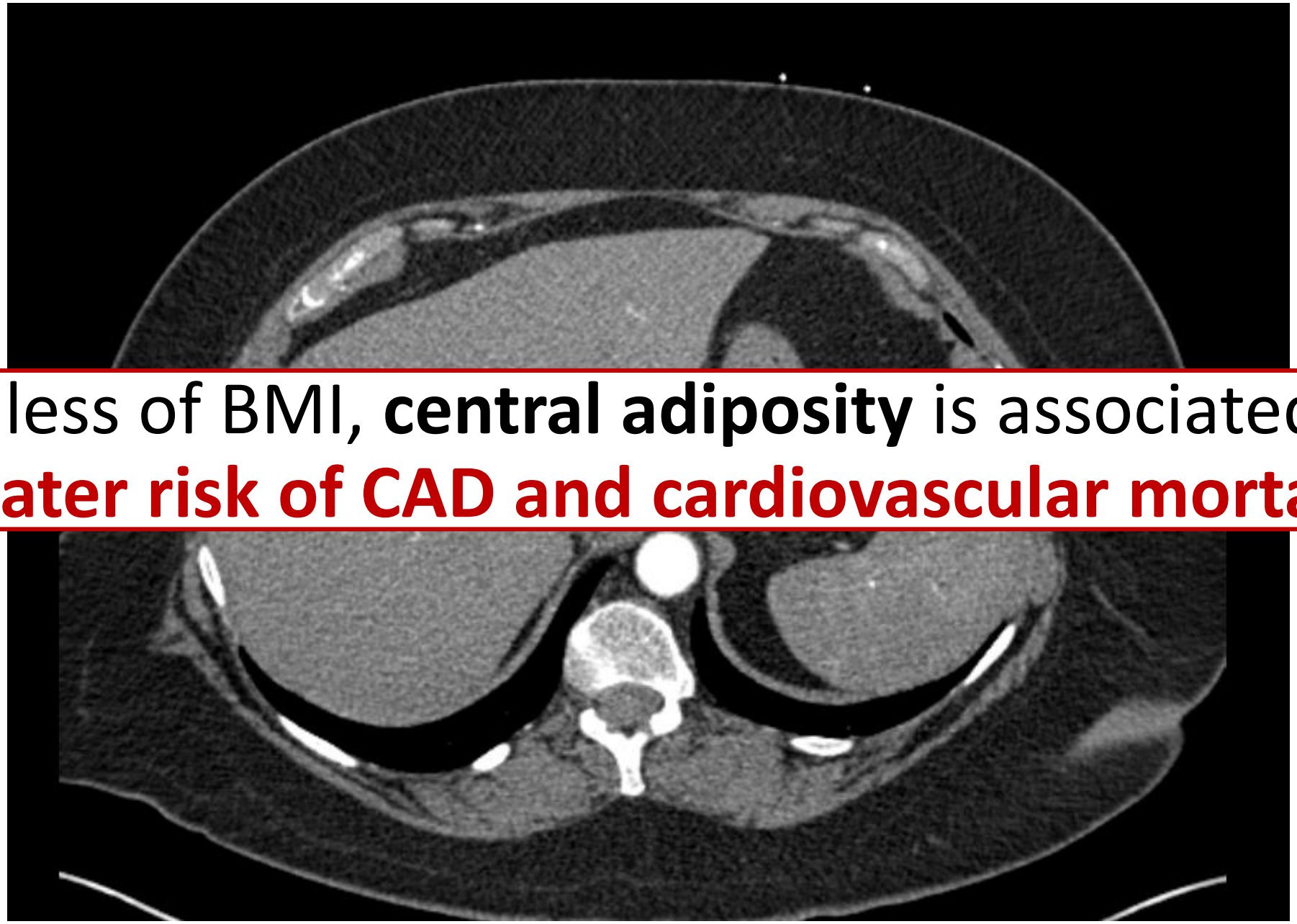
<u>Problem #1</u>: Variation by sex, age, and race/ethnicity

Circulation. 2014;129(suppl 2):S102–S138.

PROBLEM #2
BMI DOESN'T TELL YOU ABOUT CENTRAL ADIPOSITY

Waist circumference (WC):
> 102cm men and > 88cm women

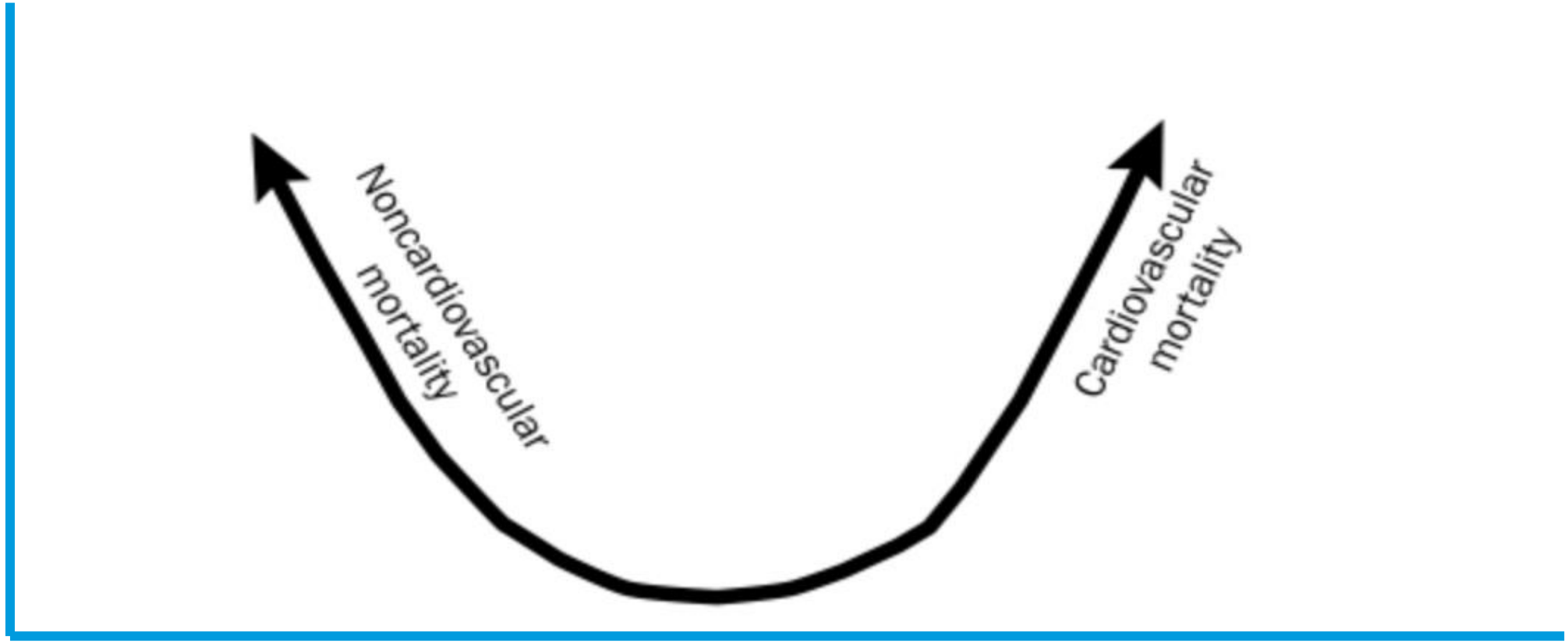
Waist to hip ratio (WHR):
≥0.90 men and ≥0.85 women



Regardless of BMI, **central adiposity** is associated with a **greater risk of CAD and cardiovascular mortality**

Circulation. 2021;143:e984–e1010

PROBLEM #3
WHAT IS THE OBESITY PARADOX?



Low BMI **Normal to Overweight BMI** **Obese BMI**

Mayo Clin Proc. 2010 Feb; 85(2): 112–114.

PROBLEM #3
OBESITY PARADOX

- Overweight or obese individuals with symptomatic CVD:
  - BMI **doesn't consistently predict** ≤10 yrs CVD outcomes

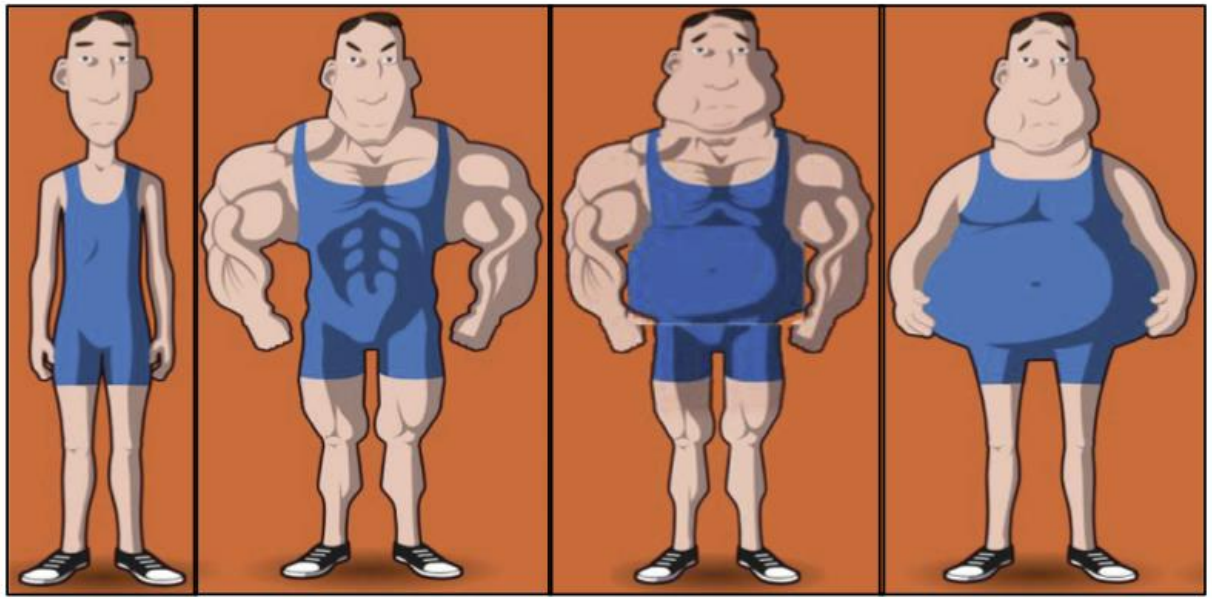
- Up to 5 years after PCI, BMI >25 kg/m2 independently predicts survival compared with normal weight

JACC Cardiovasc Interv. 2017;10:1283–1292

BODY COMPOSITION

LEAN MASS IS KEY FOR CARDIO FITNESS

Body Composition and Obesity Phenotypes



	Normal weight	Athlete	Nonsarcopenic Obese	Sarcopenic Obese
BMI (kg/m^2)	18.5-25	≥30	≥ 30	≥ 30
Fat Mass	Normal	Decreased	Increased	Increased
Lean Mass	Normal	Increased	Increased	Decreased
Cardio - Respiratory Fitness	Normal	Increased	*Mild Impairment?*	*Severe Impairment?*

Vascular Health and Risk Management 2019:15 89–100

VISCERAL ADIPOSITY
HOW TO REDUCE THIS?

150 min per week of exercise

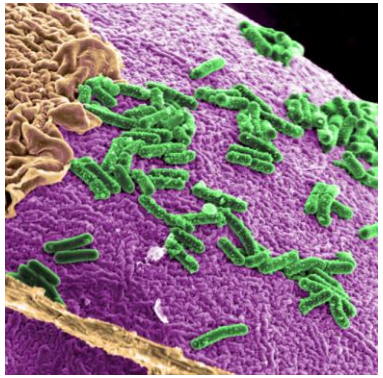
JAMA Oncol. 2015;1:766–776

HOW DOES OBESITY

CARDIOVASCULAR DISEASE?

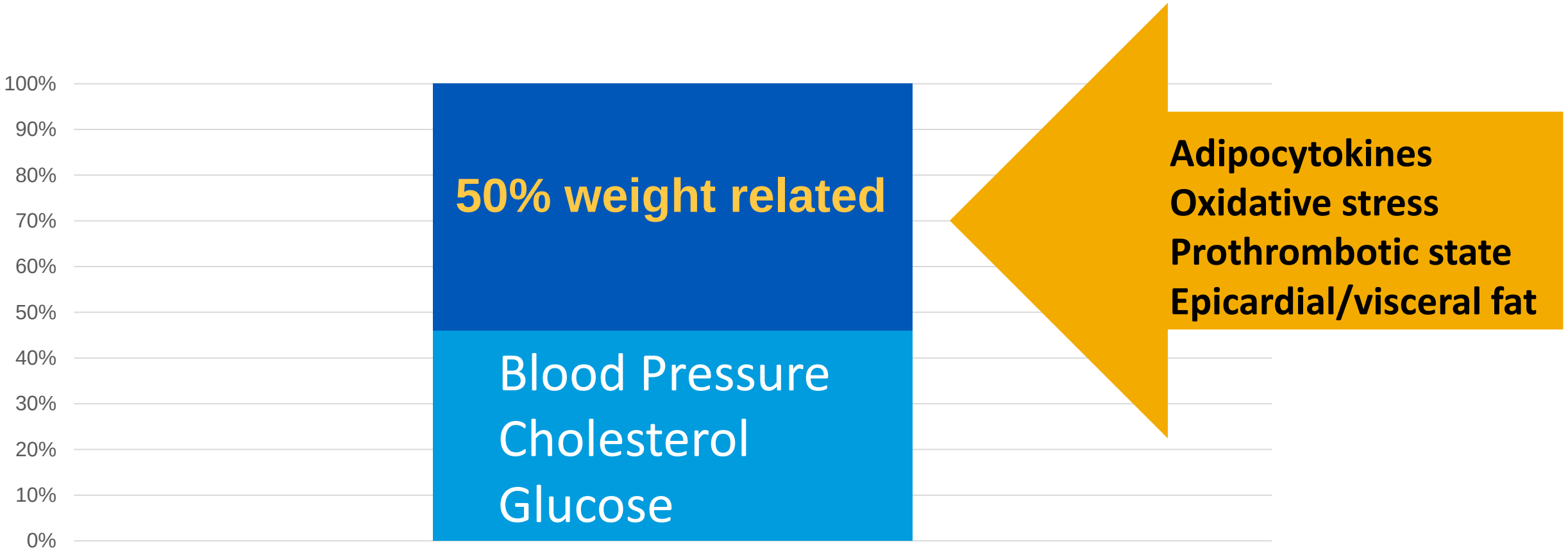
Blood Pressure
Cholesterol
Glucose

Adipocyte dysfunction
↑ Leptin
Altered lipolysis
Insulin resistance



META-ANALYSIS (21 STUDIES) OF 1.8 MILLION INDIVIDUALS

ASSOCIATIONS OF OVERWEIGHT AND OBESITY WITH CAD



Lancet. 2014;383:970–983

Obesity →Insulin Resistance → Dyslipidemia & Metabolic Syn

Adipocyte dysfunction
↑ Leptin
Altered lipolysis
Insulin resistance

Insulin resistance
↑ O_2 demand

(skeletal muscle)

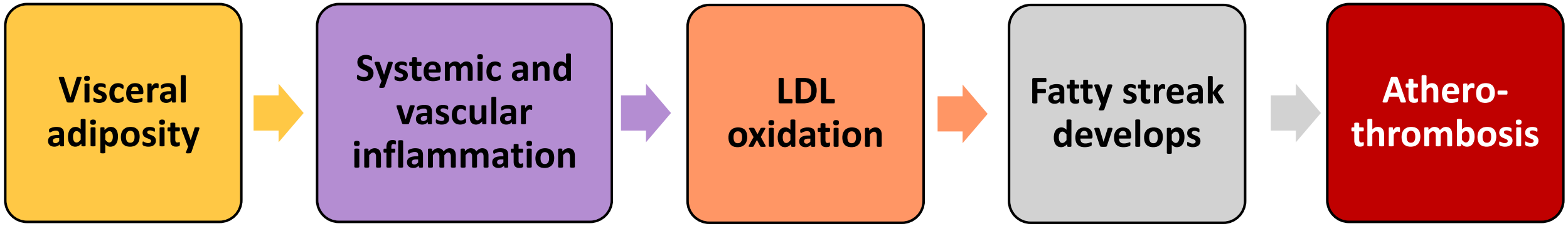
Liver steatosis

↑ De novo lipogenesis
↑ VLDL secretion
Insulin resistance

Myocardial fat deposition
Insulin resistance

(cardiac muscle)

Circulation. 2021;143:e984–e1010



Circulation. 2021;143:e984–e1010

GUT MICROBIOME AND CV DISEASE

Image from MAM

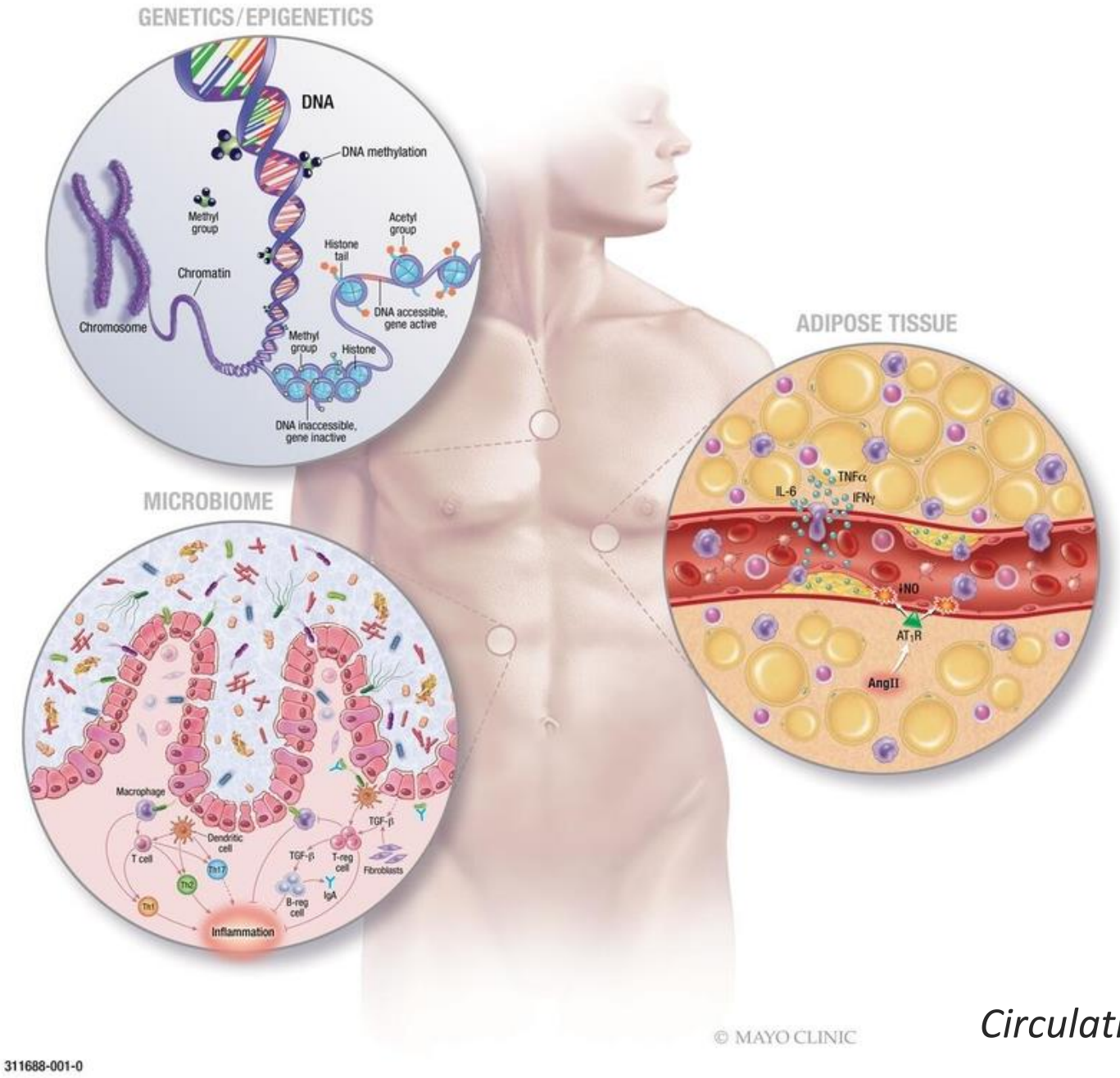


Image from MAM

Circulation 2017: 135, 1671–1673

TAKE HOME PEARLS #2

- BMI is limited as a tool
- Visceral adiposity is associated with insulin resistance and metabolic syndrome
- Influence of the gut microbiome

3 DIETARY APPROACHES FOR REDUCTION IN CARDIOVASCULAR RISK

QUESTION

- What dietary approach do you most often recommend (or what do you personally follow?)

A. Low-fat diet
B. Low-carb or ketogenic diet
C. Mediterranean diet with primarily plant protein and fish
D. Mediterranean diet with non-red meat animal protein
E. Paleo diet
F. Vegetarian
G. Vegan

Weight Loss	Diet
−0.98 to −7.05 kg	**Low-carb**
−1.75 to −2.24 kg	**Mediterranean diet**
−1.54 kg	**Low-fat diets**
−1.42 kg	**DASH diet**

Adv Nutr. 2020 Jul; 11(4): 815–833

LOW CARB/KETOGENIC DIETARY APPROACH

- Low Carb: 50–130 g/day or 10%–45% total calories
- Ketosis: Carb <20–50 g/day or < 10% total calories
- Daily protein intake 0.8–1.5 g/kg IBW
- Rest of calories from fat sources

Meta-analysis of Ketogenic diet vs Balanced Diet:
No difference in BMI or lipids (6 weeks to 24 mos)

Lopez Espinosa. Nutrients 2021: 13, 2946

LOW CARB DIET WITH ANIMAL FOOD SOURCES HIGHER ALL-CAUSE MORTALITY

- Study of 85,168 women (aged 34–59 years at baseline) and 44,548 men (aged 40–75 years at baseline)
  - Without heart disease, cancer, or diabetes
  - Followed for approx. 20 years
  - Low carb diet with either primarily animal or plant protein

Fung et al. Ann. Intern. Med. 2010; 153, 289–298

LOW CARB DIET WITH ANIMAL FOOD SOURCES HIGHER ALL-CAUSE MORTALITY

- **Low-carb diet with animal food sources**:
  - Higher all-cause mortality (HR 1.23 [CI, 1.11 to 1.37], *P* for trend = 0.051)
  - Higher CV mortality (HR, 1.14 [CI, 1.01 to 1.29]; *P* for trend = 0.029)
  - Increased cancer mortality:
    - Men 66% increased risk
    - Women 26% increased risk

Fung et al. Ann. Intern. Med. 2010; 153, 289–298

LOW CARB DIET WITH ANIMAL FOOD SOURCES HIGHER ALL-CAUSE MORTALITY

- **Low-carb diet with animal food sources**:
  - Higher all-cause mortality (HR 1.23 [CI, 1.11 to 1.37], *P* for trend = 0.051)
  - Higher CV mortality (HR, 1.14 [CI, 1.01 to 1.29]; *P* for trend = 0.029)
  - Increased cancer mortality:
    - Men 66% increased risk
    - Women 26% increased risk

- **Low-carbohydrate diet with a higher content of plant-based food:**
  - Lower all-cause mortality (HR 0.80 [CI, 0.75 to 0.85]; *P* for trend ≤ 0.001)
  - Lower CV mortality (HR 0.77 [CI, 0.68 to 0.87]; *P* for trend < 0.001)

Fung et al. Ann. Intern. Med. 2010; 153, 289–298

HIGH PROTEIN DIET

- NHANES III study of 6,381 adults ages 50+ followed for 18 years

High Protein	Mod Protein	Low Protein
20%+ calories	10-19% calories	< 10% calories

Levine et al. Cell Metab. 2014:19, 407–417.

HIGH PROTEIN DIET

Ages 50–65

High protein intake

- 74% increase all-cause mortality (HR: 1.74; 95% CI: 1.02–2.97)
- 4X risk of cancer mortality (HR 4.33; 95% CI: 1.96–9.56)
- If plant protein was used instead of animal, no increased risk

Ages > 65 with

High protein intake

- 28% reduction in all-cause mortality (HR: 0.72; 95% CI: 0.55–0.94)
- 60% reduction in cancer mortality (HR: 0.40; 95% CI: 0.23–0.71)

Levine et al. Cell Metab. 2

VEGAN & VEGETARIAN DIETS

- Reduced risk of cancer, hypertension, diabetes
- Less greenhouse emissions gas for equicaloric diet
- Increased risk of fractures
- Balancing adequate protein especially > 65 years
- Can be difficult for patients to follow life-long

Segiovia-Siapco et al. Eur. J. Clin. Nutr. 2019;72, 60–70.

MEDITERRANEAN DIET

MEDITERRANEAN DIET

More of:

- ✓Vegetables & fruits
- ✓Whole grains
- ✓Plant-based protein
- ✓Fish

Limit:

- ✓ Sugar,
- ✓ Sodium
- ✓ Red and processed meat

Diet	MACE	Hazard Raio
Mediterranean+Nuts	3.4%	0.72 (95% CI, 0.54-0.95)
Mediterranean Olive Oil	3.8%	0.69 (95% CI, 0.53-0.91)

N Engl J Med 2018; 378:e34

Eur J Clin Nutr. 2018;72:30–43

INTERMITTENT FASTING

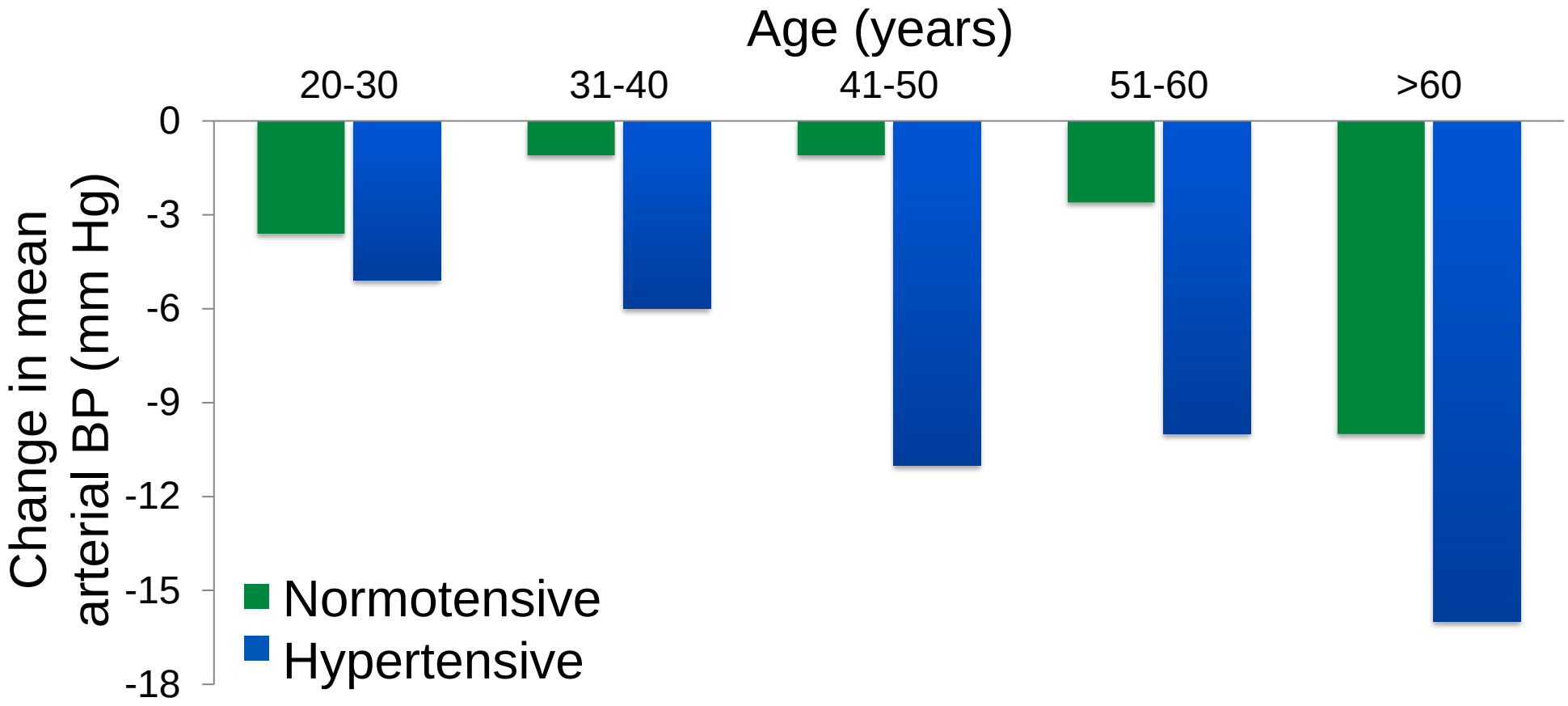
- TRE: time restricted eating
  - Weight loss of 7-11 pounds over 10 weeks
- Alternative day fasting
- 5:2 schedule of days eating:fasting
- Periodic fasting (2-5 days intermittently)

Longo et al. Cell 2022: 185:1455

LOW SODIUM DIET

MEAN ARTERIAL BP ↓ WITH SALT RESTRICTION

BASED ON AGE AND AVERAGE BP



Hypertension. 2016;68:00-00.

NUTRITION AND LONGEVITY

Genetics
Size
Age
Sex
Health

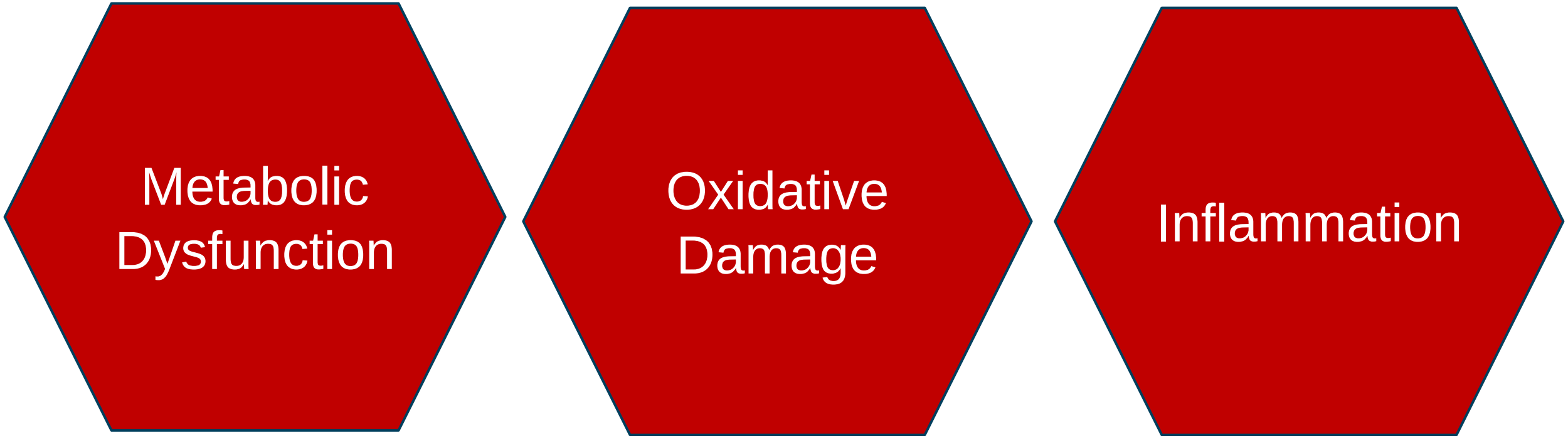
Nutrient Responsive Genes/Pathways

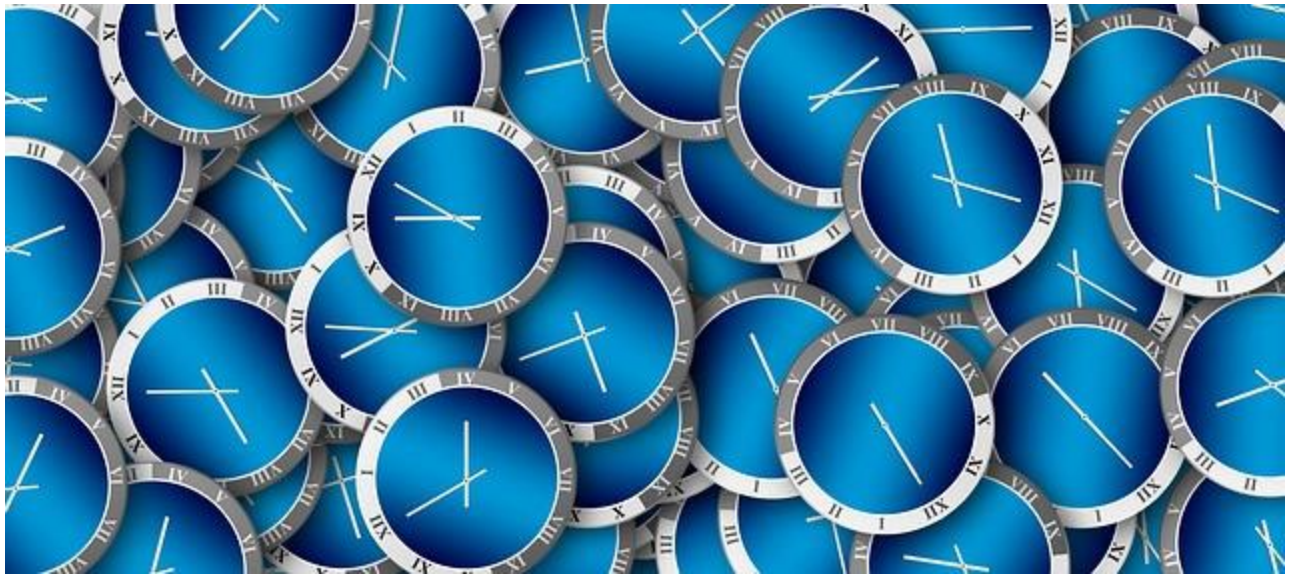
Autophagy
Mitochondrial function
Translation
RNA processing
Stress response

Altering the Quantity or Type of Nutrients

Eating Patterns

WE WANT TO STOP…





8 YEARS

MODELING STUDY OF FOOD CHOICES ON LIFE EXPECTANCY

- Optimal diet:
  - Legumes
  - Whole grains
  - Nuts
  - Reduced red and processed meats

<u>Started age 20</u> = Increased life expectancy +10.7 yrs females and +13 yrs in males

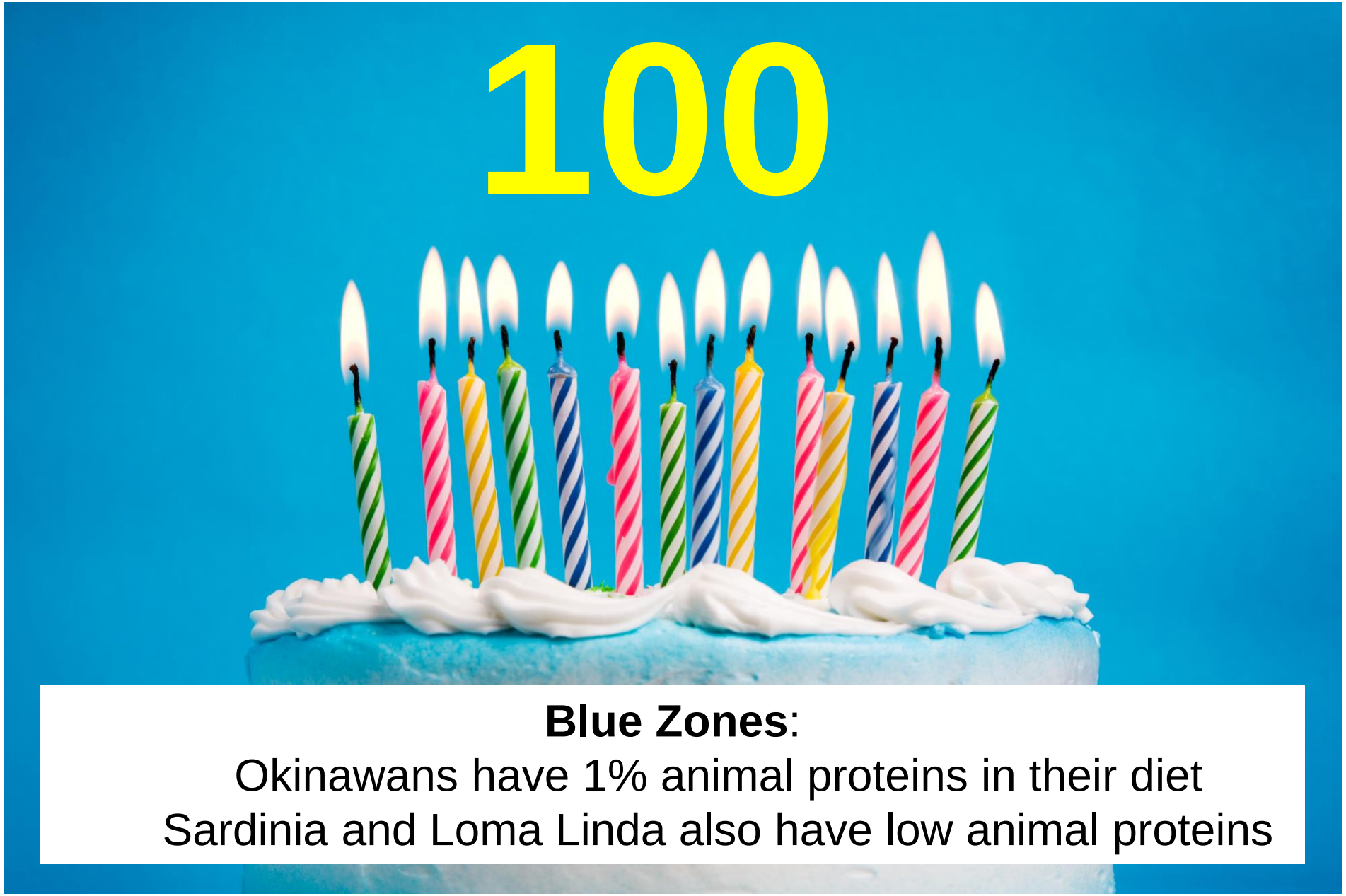
<u>Started age 60</u> = Increased life expectancy +8 yrs

Fadnes et al. PLOS 2022

LONGEVITY DIET

- Mid to high complex carbohydrates
- Low but sufficient protein intake (pesco-vegetarian-derived proteins)
  - Maybe higher protein > 65 years
- 30% healthy fat sources
- 12-13 hour daily fasting

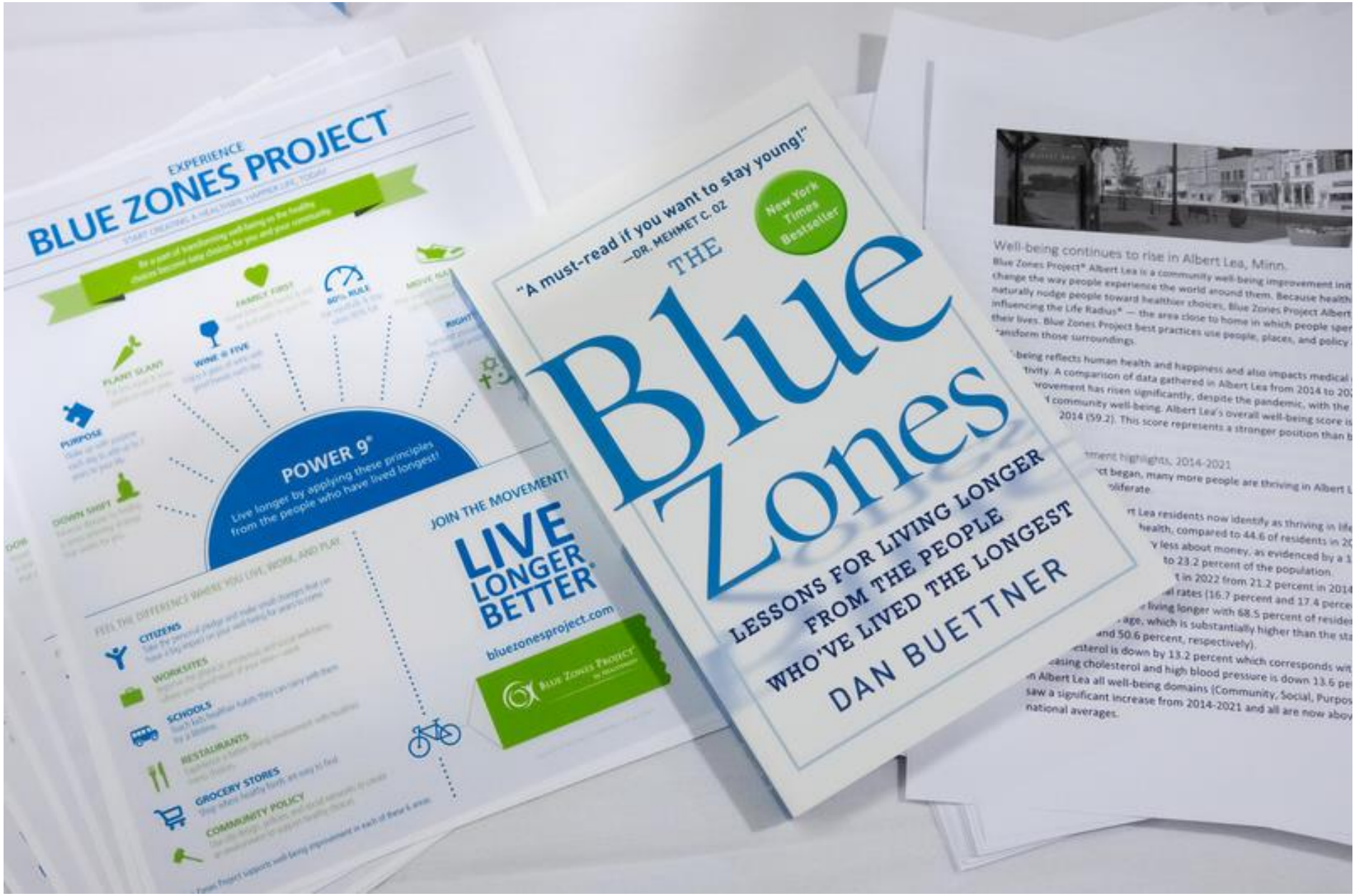
Longo et al. Cell 2022: 185:1455



Blue Zones:

Okinawans have 1% animal proteins in their diet

Sardinia and Loma Linda also have low animal proteins



#1

Move Naturally

#2

Purpose

#3

Down-shift

#4

80% Rule

#5

Plant Slant

#6

Wine at 5

#7

Right Tribe

#8

Loved Ones First

#9

Belong

TAKE HOME PEARLS #3

- Mediterranean diet reduces cardiovascular events
- Blue Zones 9 principles are more than just diet alone and are a blueprint for longevity

4 OVERALL APPROACH FOR HEART HEALTH

LIFE'S ESSENTIAL 8

Health Behaviors

Health Factors

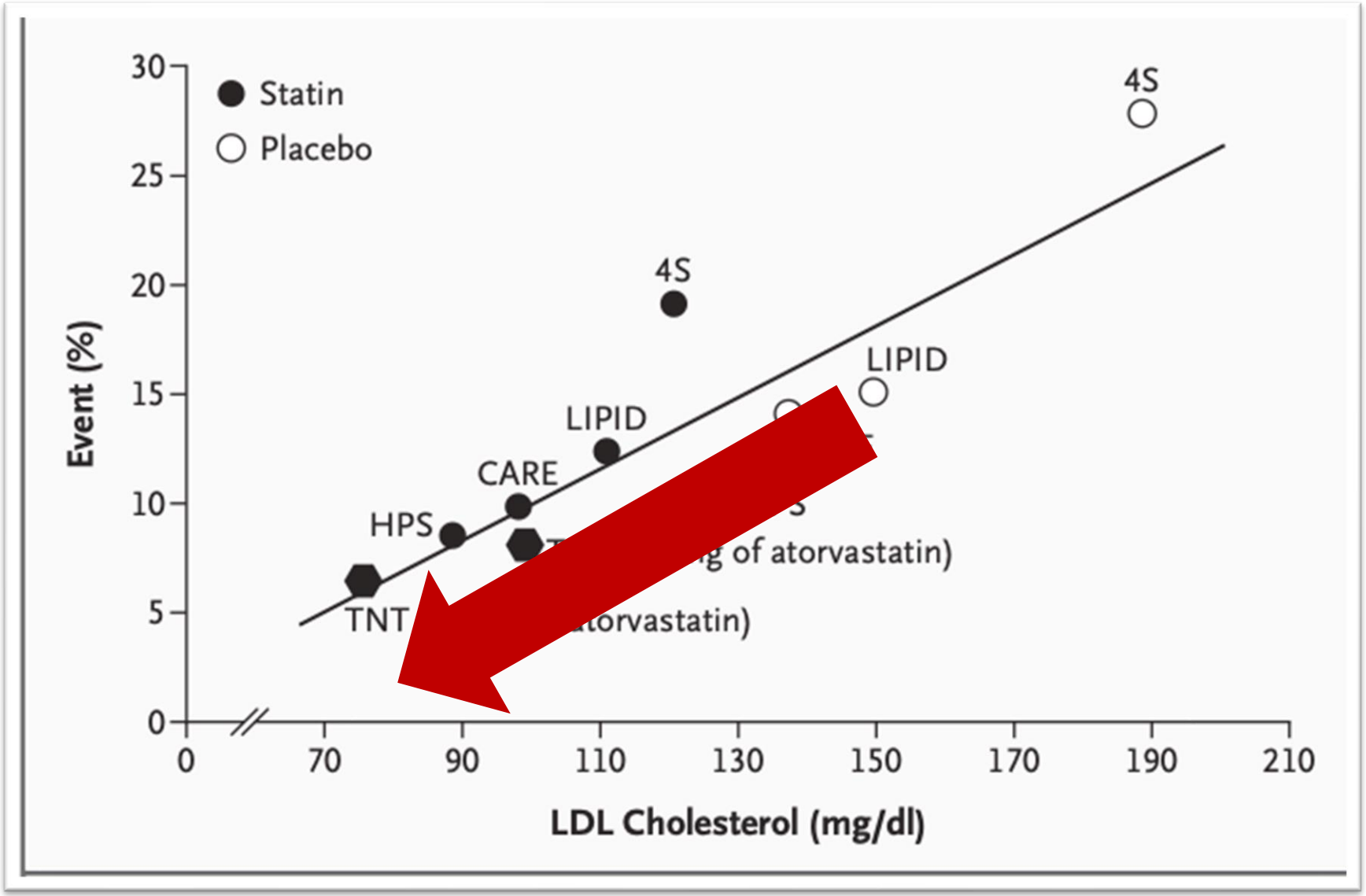
www.Heart.org

TAKE HOME PEARLS #4

- Blood pressure > 130/80 HTN
- Blood sugar control
- Exercise 150 minutes/week
- No tobacco products
- Importance of sleep

5 WHEN LIFESTYLE ALONE IS ENOUGH AND MEDS ARE NEEDED

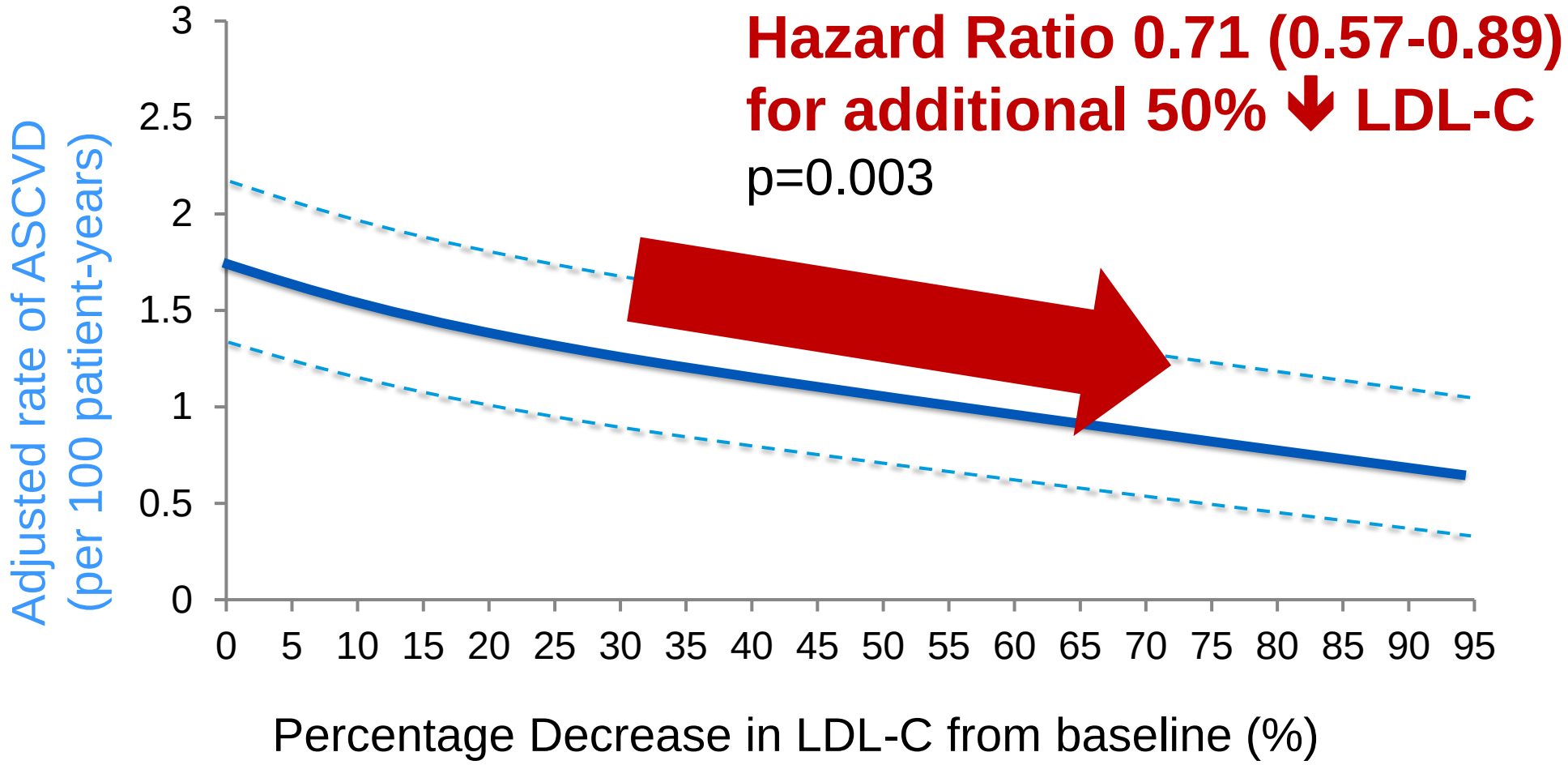
LOWER LDL → LOWER EVENT RATES



NEJM 2005;352:1425

Slide courtesy of Dr. Scott Wright

FEWER ASCVD EVENTS WITH LOWER LDL *(% CHANGE FROM BASELINE)*



Ray K, et al. J Am Coll Cardiol. 2016;67(13_S):2082-2082

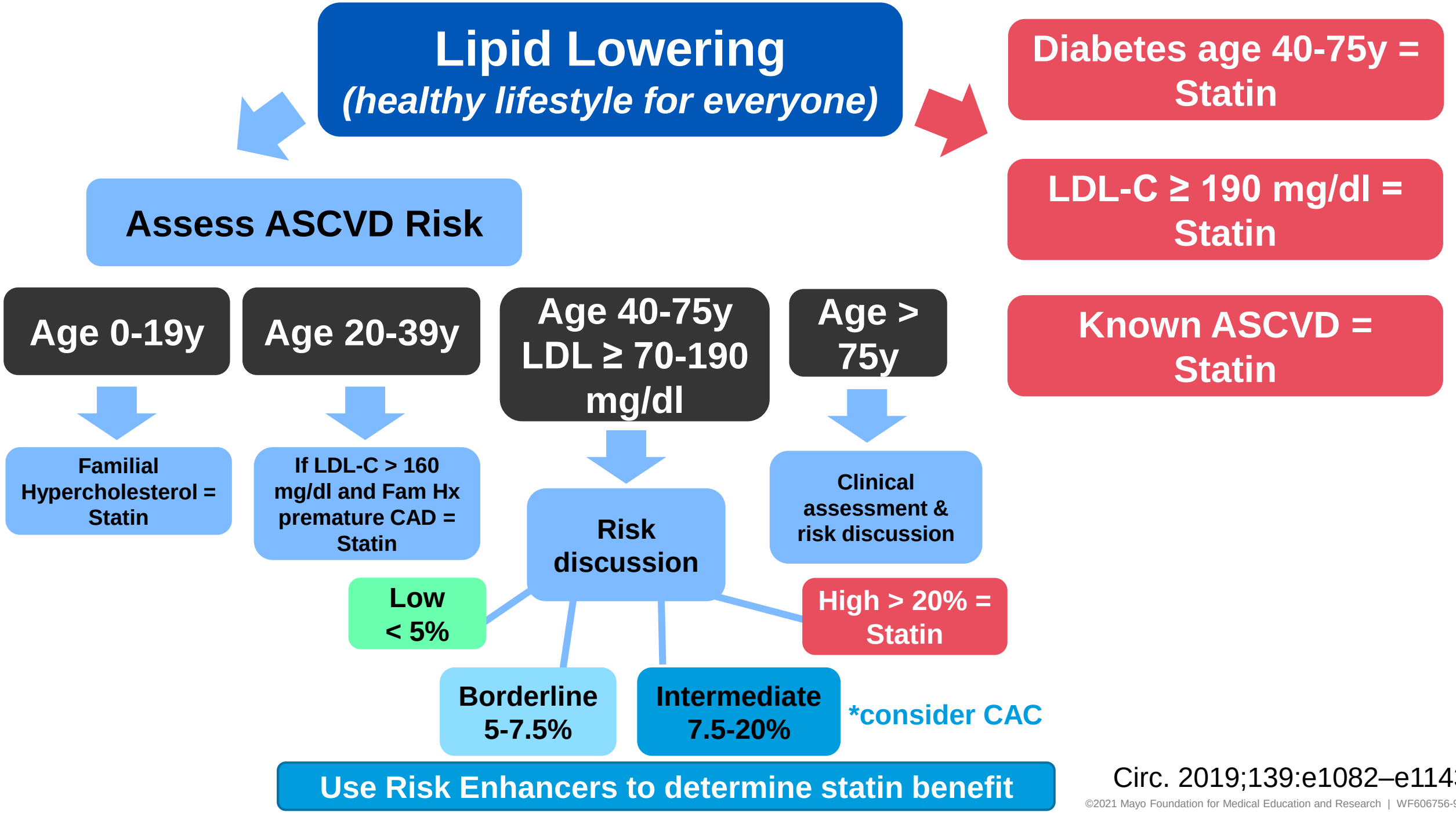
Statins

Ezetimibe

Bempedoic Acid

PCSK9i Monoclonal Antibody

PCKS9i Small Interfering RNA



Circ. 2019;139:e1082–e1143

Very high-risk ASCVD

2+ ASCVD events or
1 major event with high-risk conditions

< 50% LDL reduction and LDL-C ≥ 55 mg/dL
consider adding nonstatins
to max tolerated statins

Ezetimibe

PCSK9 Inhibitor

JACC 2022;80:1366-1418
Circulation. 2019;139:e1082–e1143

VERY HIGH RISK FOR FUTURE ASCVD EVENTS

Major ASCVD Events	High-Risk Conditions
ACS within last 12 months	≥ 65 years old
Myocardial infarction	Familial hyperlipidemia
Ischemic stroke	CABG or PCI
Symptomatic PAD	Diabetes
Amputation or prior revasc	HTN
	CKD eGFR < 60 ml/min/1.73m2
	Tobacco use current
	LDL > 100 on max statin + ezetimibe
	CHF

Very High Risk =

❑ 2 Major ASCVD

❑ 1 Major + 2 High-Risk Conditions

Circulation.2019;11:e563-e595

BACK TO OUR PATIENT

- She was started on rosuvastatin 20mg daily and Evolocumab with goal LDL < 55 mg/dl
- Started aspirin for symptomatic PAD
- Counseled regarding tobacco cessation options
- PET Stress showed normal perfusion
- Began a supervised exercise training program (SET) for her new diagnosis of PAD

ASCVD (but not very high risk)

< 50% LDL reduction and LDL-C ≥ 70 mg/dL
consider adding nonstatins
to max tolerated statins

Ezetimibe

PCSK9 Inhibitor

JACC 2022;80:1366-1418
Circulation. 2019;139:e1082–e1143

ASCVD +
Severe primary hyperlipidemia
LDL-C ≥ 190mg/dL

Begin high-intensity statin, if LDL-C remains ≥ 70 mg/dL
consider adding nonstatins

- Ezetimibe
- PCSK9 Inhibitor

JACC 2022;80:1366-1418
Circulation. 2019;139:e1082–e1143

Severe primary hyperlipidemia
LDL-C ≥ 190mg/dL

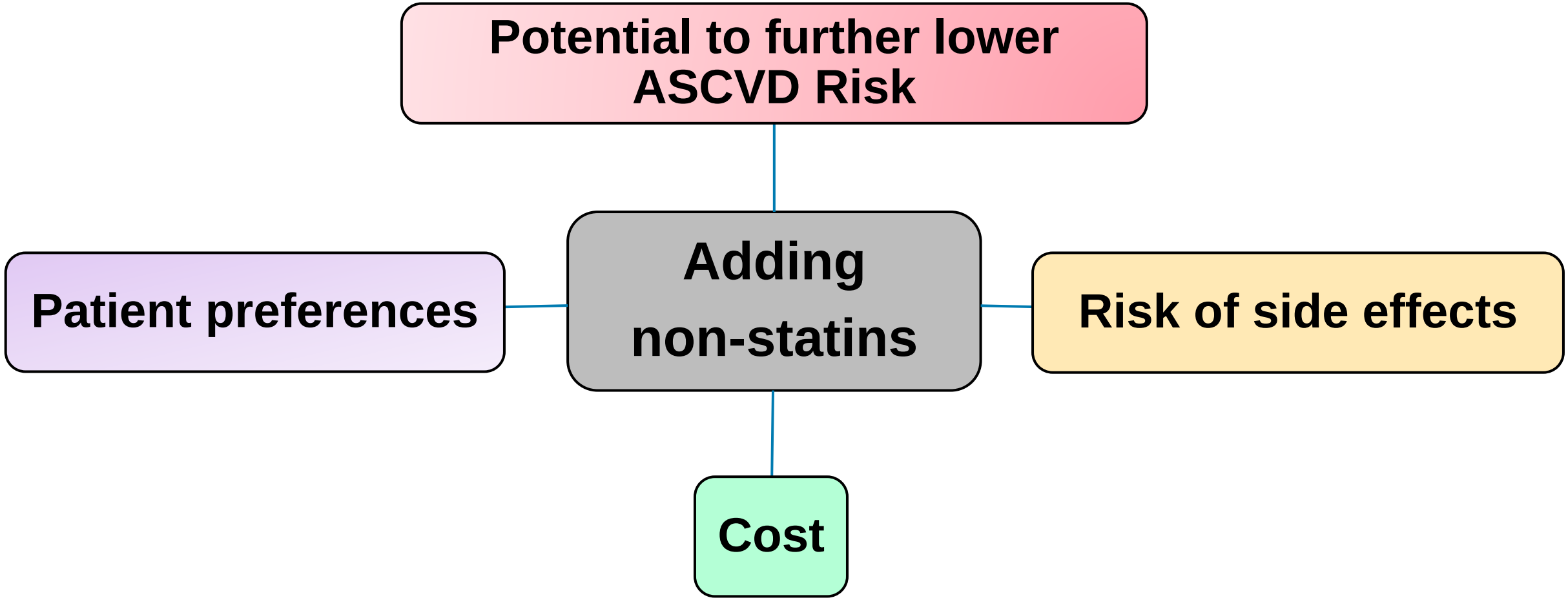
Begin high-intensity statin, if LDL-C remains ≥ 100 mg/dL
consider adding nonstatins

Ezetimibe

PCSK9 Inhibitor

JACC 2022;80:1366-1418
Circulation. 2019;139:e1082–e1143

2022 ACC EXPERT CONSENSUS ON NON-STATIN MANAGEMENT OF LDL CHOLESTEROL



JACC 2022;80:1366-1418

TAKE HOME PEARLS #5

- In general, no LDL “floor” for how low for CV risk reduction
- Lower LDL = lower event rates
- Risk stratify based on Very High Risk for LDL < 55 mg/dl

WHAT WE HAVE DISCUSSED
INTEGRATING RISK FACTORS AND HEALTHY LIFESTYLE APPROACHES

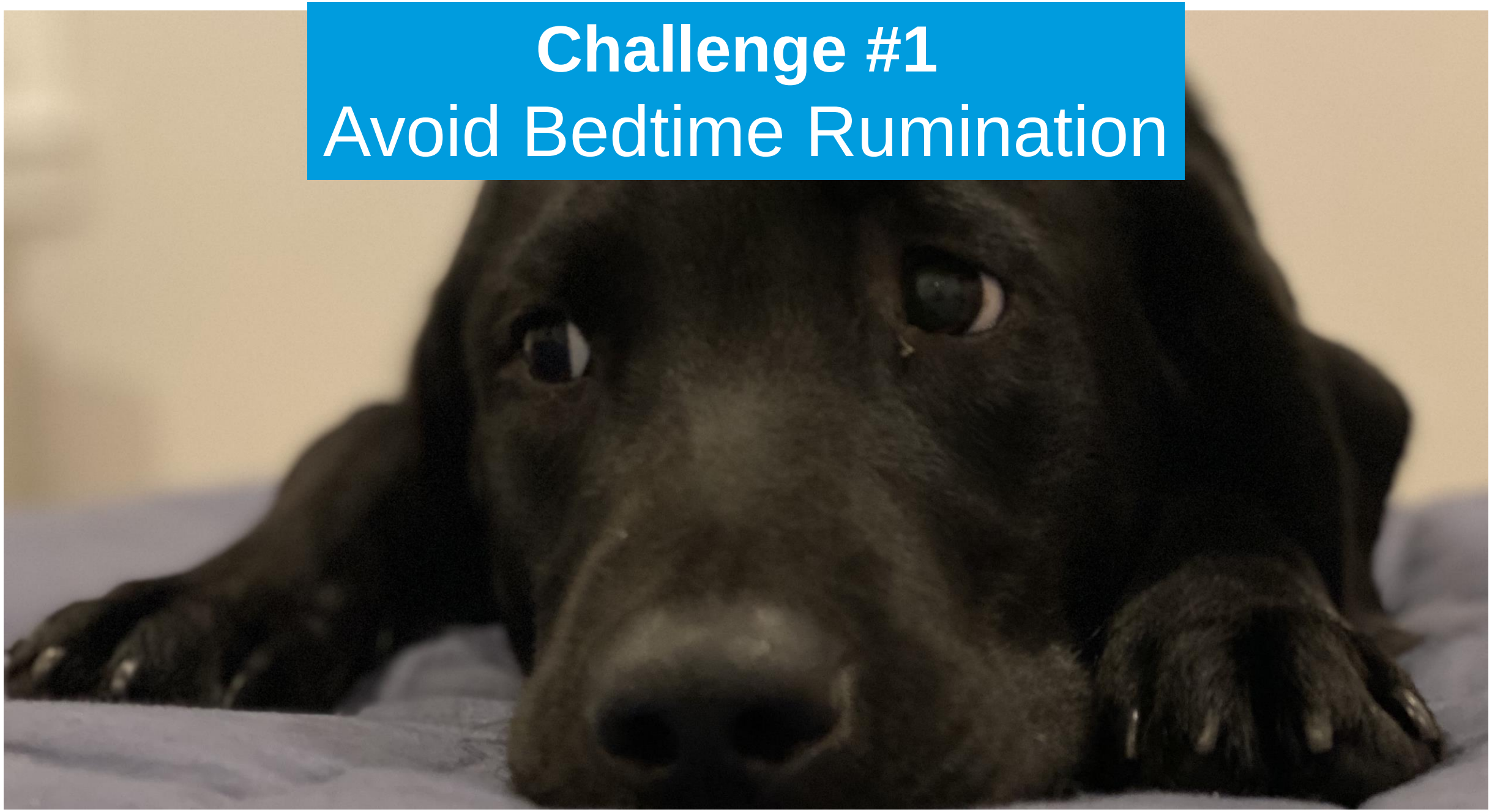
- Individualize cardiovascular risk
- Weight management isn’t just calories in < calories out
- Dietary approaches for reduction in cardiovascular risk
- Overall approach for heart health
- When lifestyle alone isn’t enough and meds are needed

TAKE HOME MESSAGES
HOW TO EAT HEALTHY FOR A LIFETIME

- Mediterranean diet (Longevity diet) that is high in plants/plant protein with fish and low in other animal proteins
- Low in sugar and simple carbs
- Overnight fast for 12-13 hours
- Enjoy the birthday cake or celebratory foods
- Low salt
- 9 Blue Zone Principles of Living

WHO LIKES A CHALLENGE?

Challenge #1
Avoid Bedtime Rumination




Challenge #2
Remember to Breathe

Challenge #3
Start the Day on Your Terms

Challenge #4
Embrace Life's Simple Joys

Challenge #5
Connect with Friends and Family

THANK YOU!

pollak.amy@mayo.edu