



# CARDI•OH

Ohio Cardiovascular and Diabetes Health Collaborative



In partnership with:



## Cardi-OH ECHO

# *Health Equity and Cardiovascular Risk*

October 26, 2023



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# Today's Presenters



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# Disclosure Statements



- The following speakers and subject matter experts have a relevant financial interest or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of their presentation\*:
  - Danette Conklin, PhD; Kathleen Dungan, MD, MPH; Adam T. Perzynski, PhD; Christopher A. Taylor, PhD, RDN, LD, FAND; Jackson Wright, MD, PhD
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\* These financial relationships are outside the presented work.

\*\* For more information about exemptions or details, see [www.acme.org/standards](http://www.acme.org/standards)



# Cardiovascular Risk and Menopause

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# Learning Objectives



- 1) Describe changes in cardiovascular risk among women experiencing menopause.
- 2) List and describe key elements of a clinical evaluation for menopausal women that are unique to this population.
- 3) Describe interventions to reduce CVD risks for per- and postmenopausal women.

# WHO Facts



- 1975 → 2016 OBESITY PREVALANCE TRIPLED
- Most of the world's population live in countries where overweight and obesity kills MORE people than underweight.
- No longer just a high-income country problem.



## World-Wide:



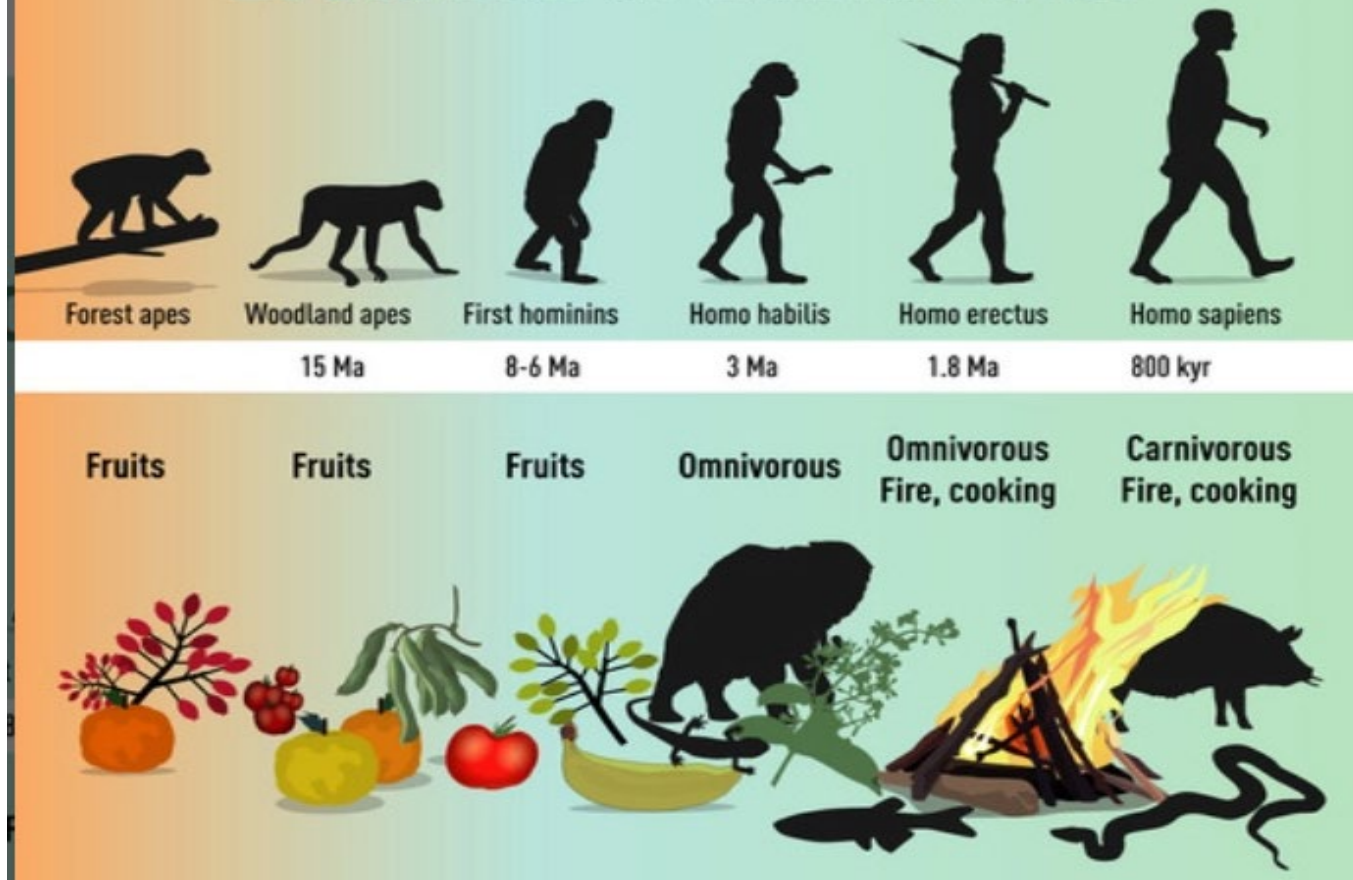
Obesity:  
671 Million

Cardiovascular  
Disease:  
523 Million

Type 2 Diabetes:  
439 Million

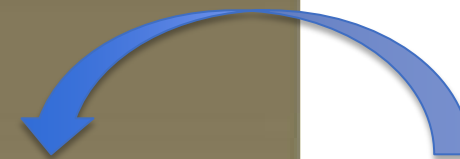


# Evolution of human diet

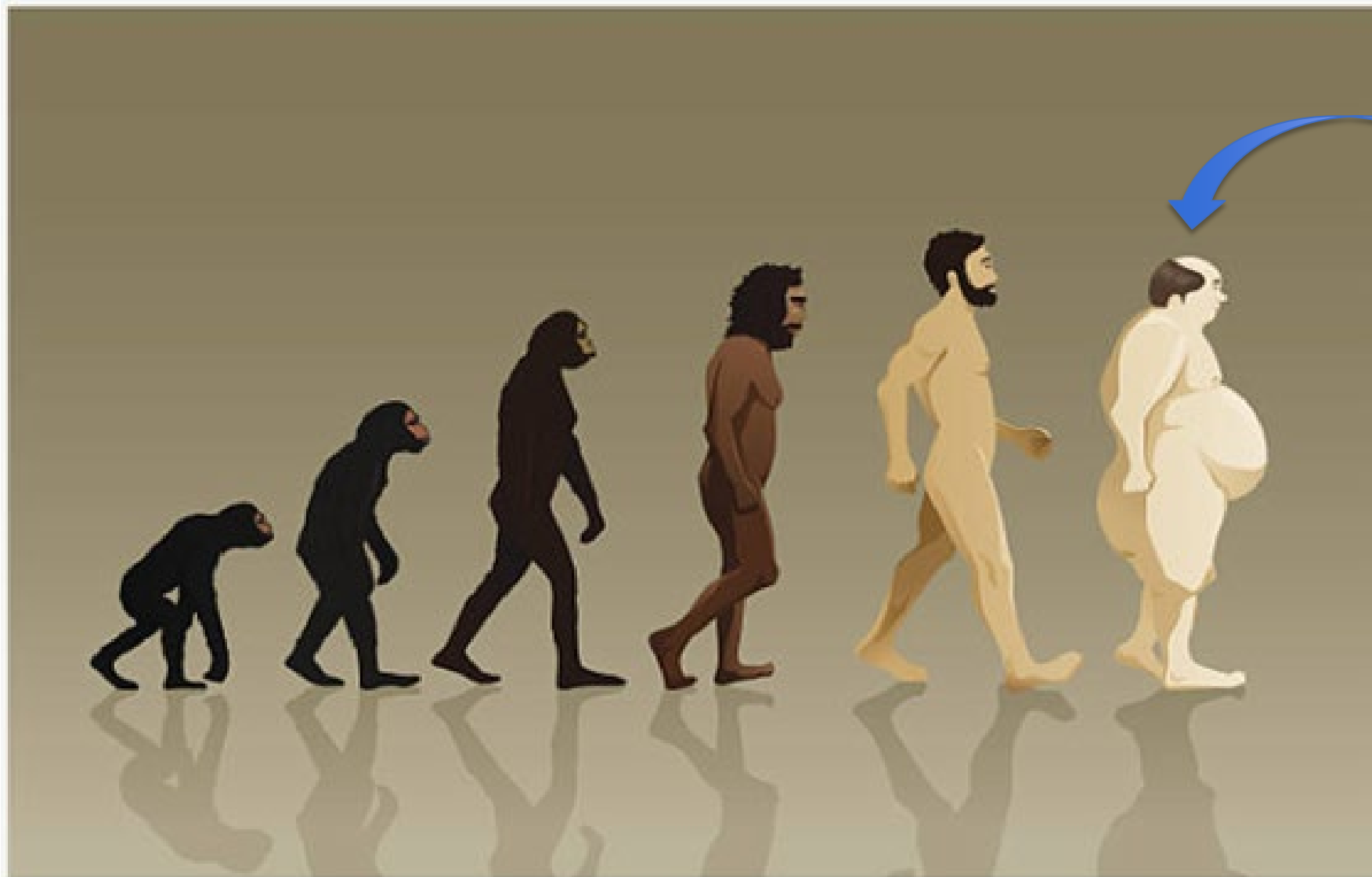


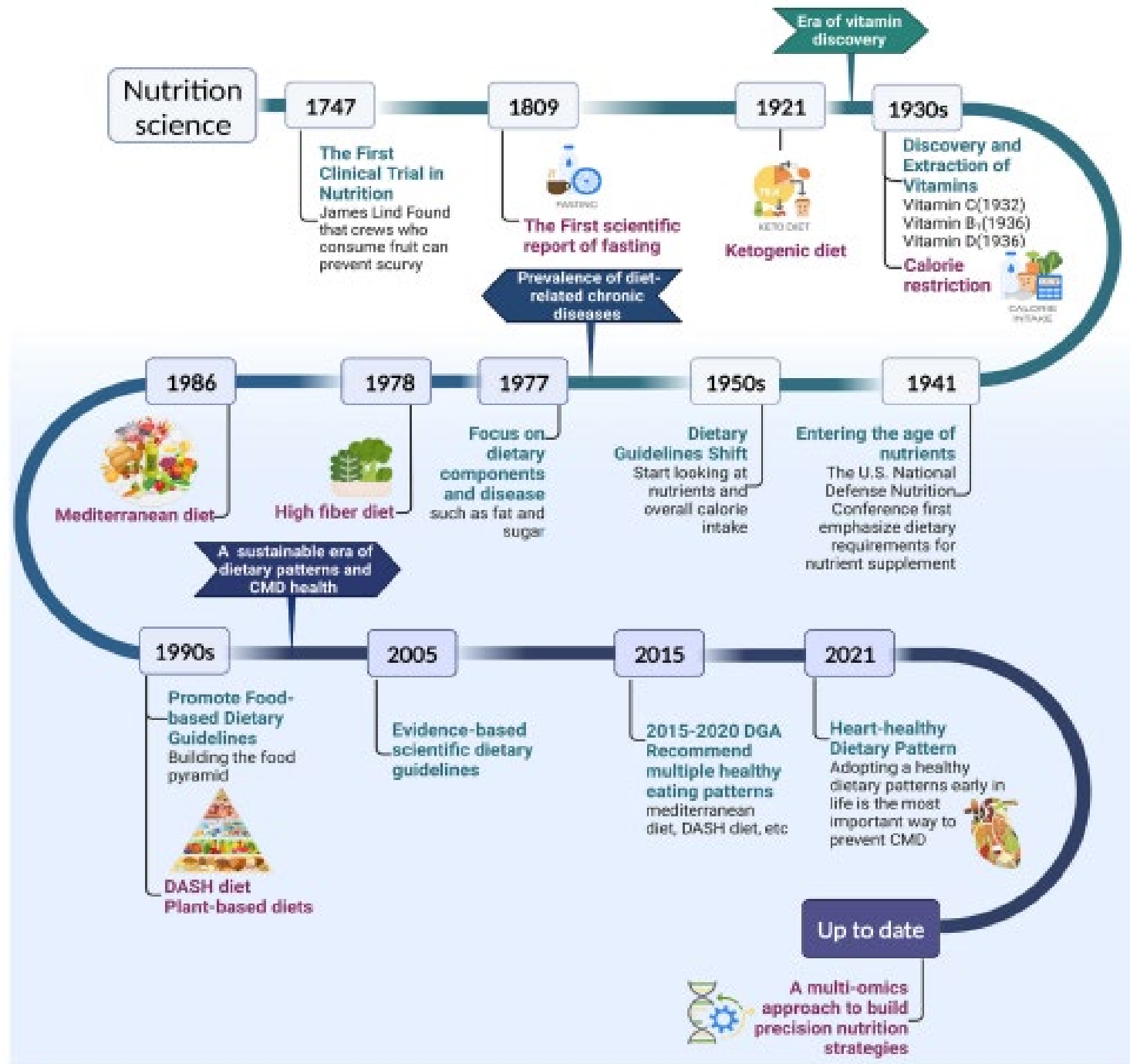


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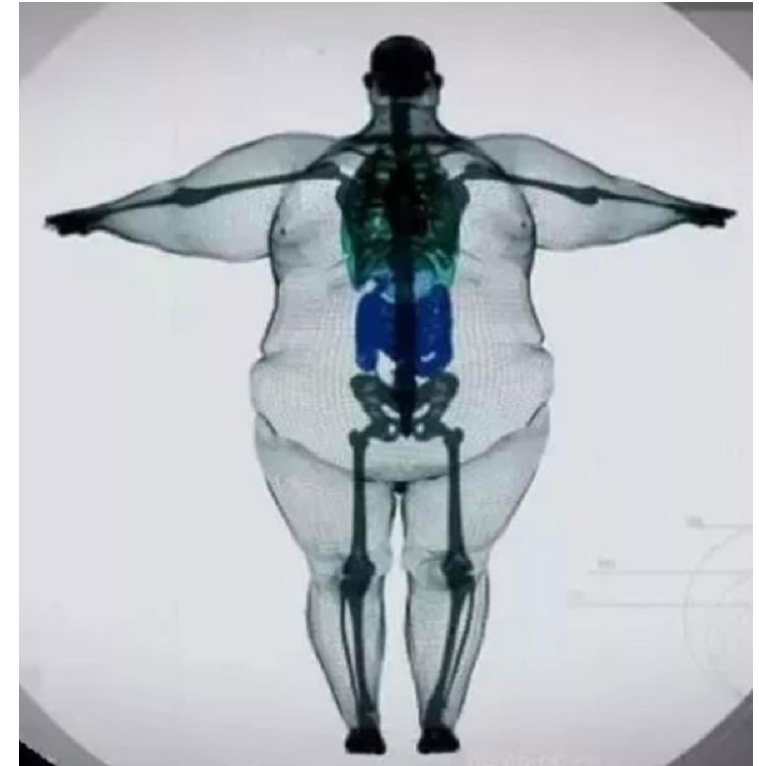
2023





# Heart Disease Risk Factors

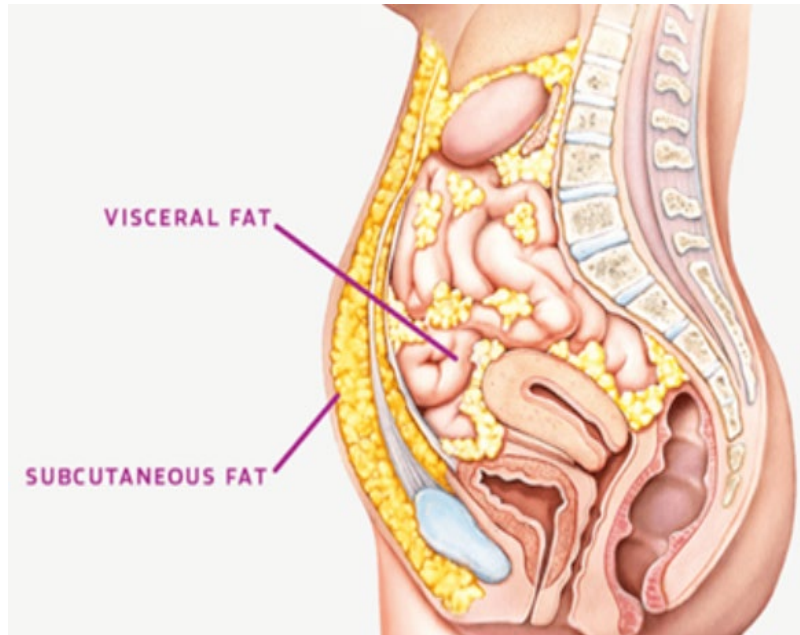
- ~2,200 adults die daily in the US due to Cardiovascular Disease (CVD)
- Obesity increases the risk of CVD by ~two-fold.
- Heart Disease and Stroke risk factors:
  - Unhealthy diet
  - Visceral adiposity
  - Physical inactivity & sedentary lifestyle
  - Tobacco use
  - Harmful use of alcohol



Visceral Adiposity



# The Metabolic Syndrome



Hypertension

Dyslipidemia

Cardiovascular Disease

Type 2 Diabetes

Non-alcoholic fatty liver disease

Several cancers

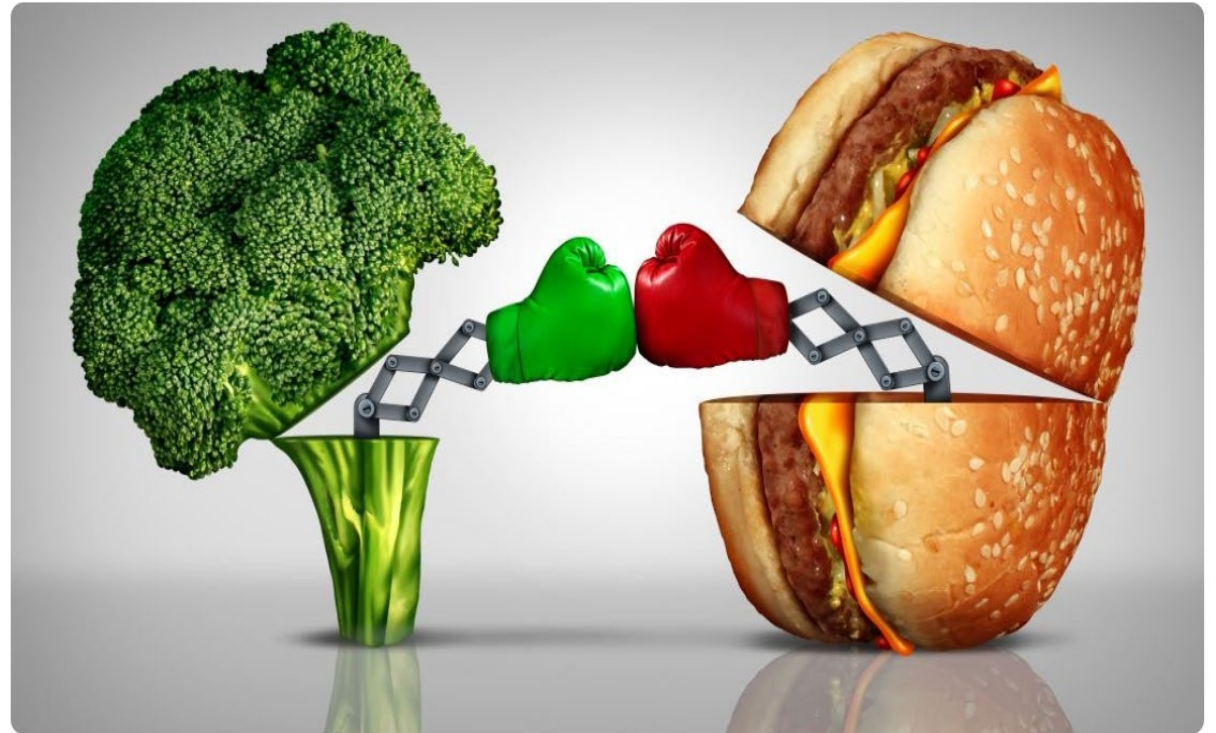
# Unhealthy Nutrition Habits

- Added sugars
- Excessive salt
- Refined foods
- Unhealthy fats
- Low intake of: vegetables, fruits, whole grains, fibers, fish and nuts



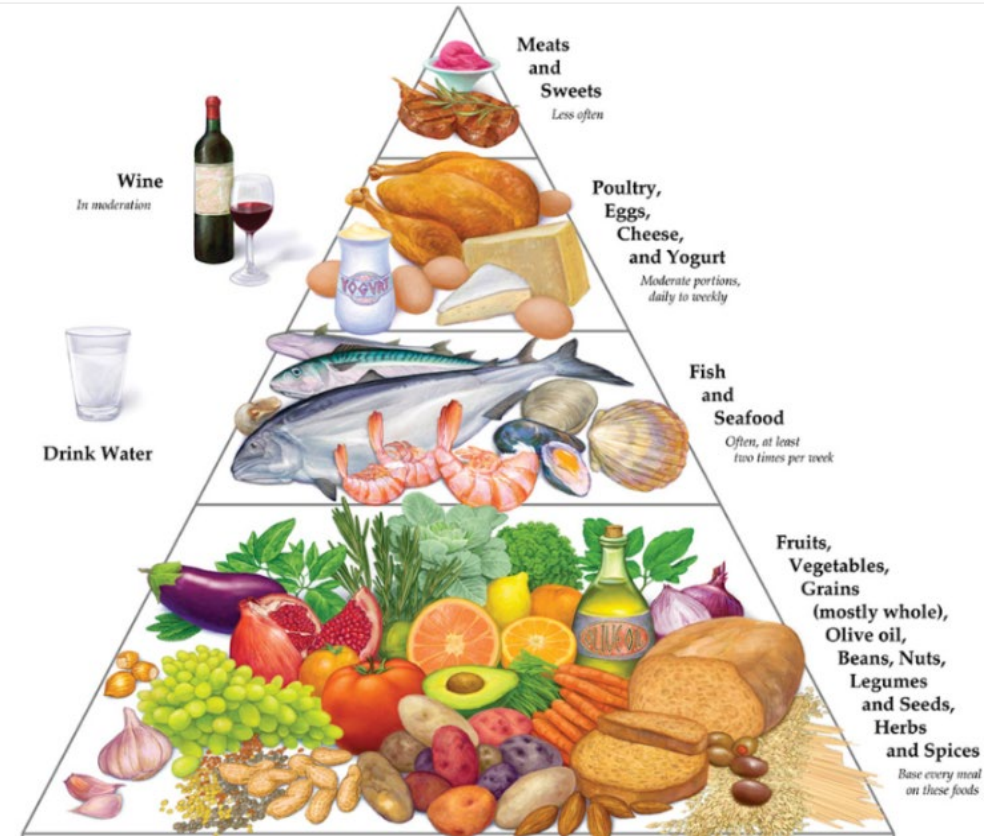
# Dietary Interventions that Impact CVD

- Calorie Restriction
- Fat Restriction
- The Mediterranean Diet
- The DASH Diet
- The Ketogenic Diet
- Plant Based Diet
- Intermittent Fasting



# The Mediterranean Diet

- **High intake:**
  - Vegetables and whole-grain cereals
  - Extra virgin olive oil, fruit, tree-nuts,
- **Moderate intake:**
  - Fish and poultry, wine
- **Low intake:**
  - Dairy, red meat (twice/month), processed meats, and sweets



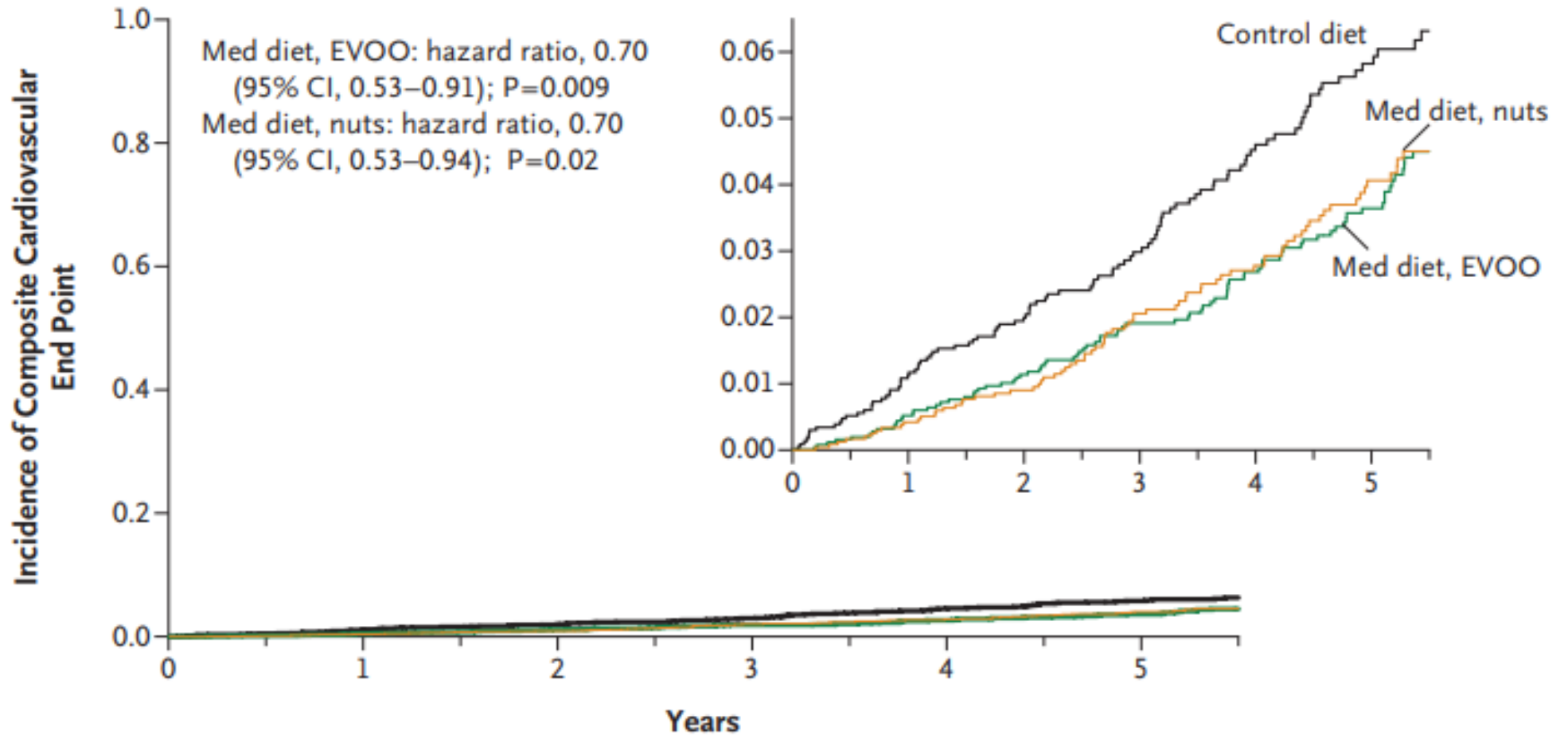


# PREDIMED Study: The Mediterranean Diet



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## A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)



NEJM

# Menopausal Transition

Depletion of ovarian follicles



Decreased ovarian follicle responsiveness to the pituitary gonadotropins (FSH & LH)



Lower serum levels of ovarian hormones Estrogen and Progesterone



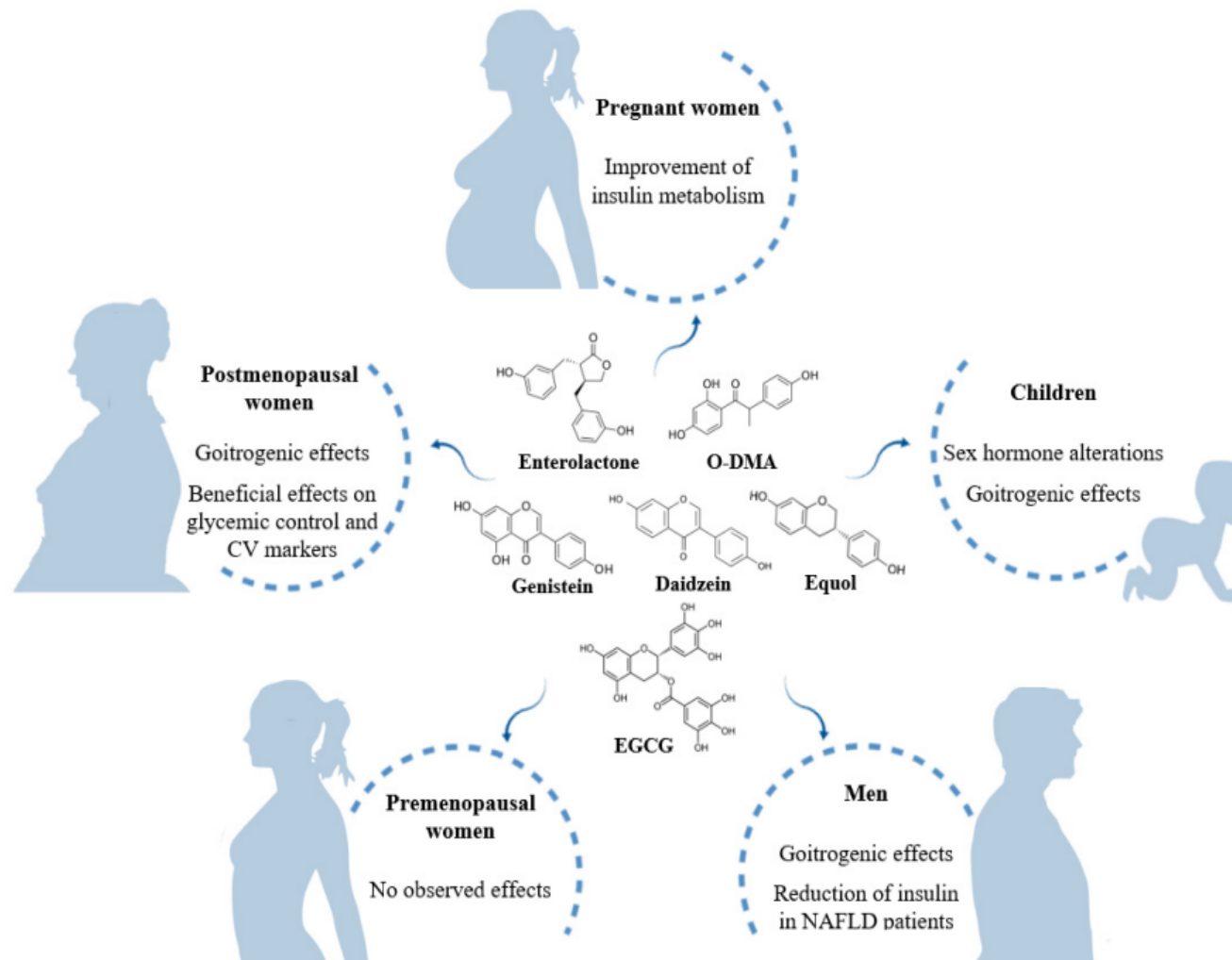
Vasomotor symptoms, hot flashes, vaginal dryness

Osteoporosis, CV disease, and breast cancer

# The Mediterranean Diet and Menopause



- Severity of menopausal symptoms have been shown to have an inverse association with adherence to the MD.
- The intake of legumes and EVOO was associated with lower severity of menopausal and psychological symptoms.
- Soy intake (known as a legume) has been shown to help
  - Soy → isoflavones → chemical structure resembling estrogens.
- Dietary phytoestrogens are bioactive compounds with estrogenic activity



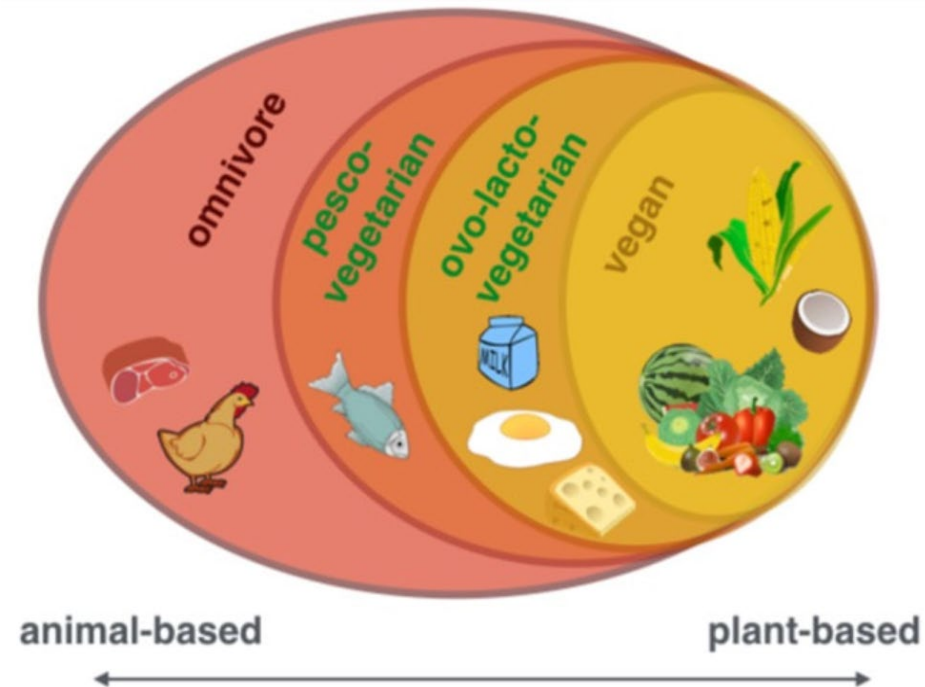
**Figure 3.** Summary of the effects of dietary phytoestrogens at different life stages. NAFLD: non-alcoholic fatty liver disease.

**BUT – Evidence of the effect of Phytoestrogens on the Endocrine biomarkers is inconclusive**

# Plant-Based Diets

- Characterized by the intake of plant products and reduction or elimination of animal-based food.

- Subcategories:



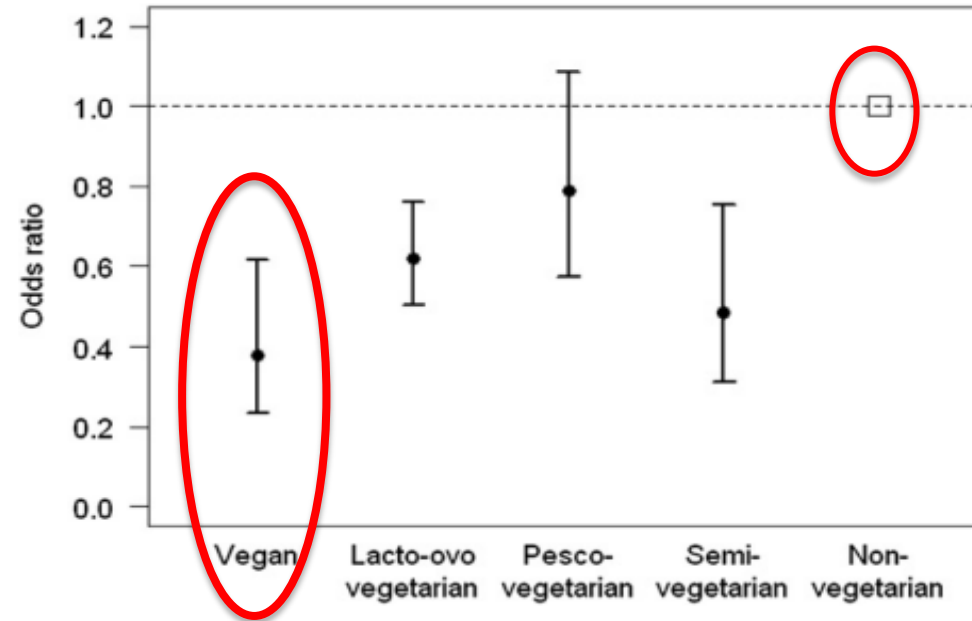
# Plant-Based Diets

- Large prospective cohort studies: vegetarians exhibit:
  1. Lower all-cause mortality
  2. CV-related mortality
  3. Less cardiometabolic risk than meat eaters
  
- May reduce risk of :
  - Coronary heart disease events by ~40%,
  - Risk of Cerebral vascular disease by ~29%



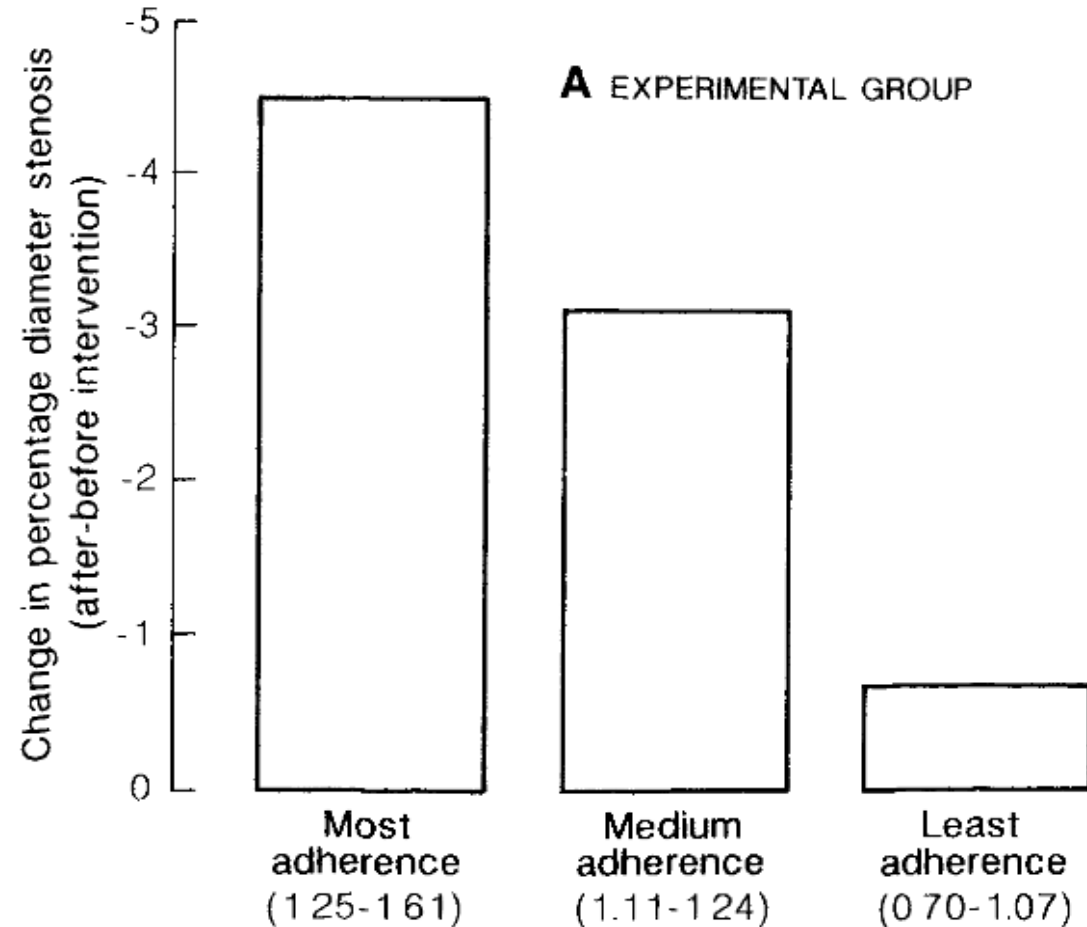
# Adventist Health Study-2

- Vegan patients had a 77% risk reduction in developing diabetes



**Figure 1** Odds ratios with 95% confidence intervals for incident diabetes by dietary group adjusted for age, BMI, ethnicity, gender, educational level, income, TV watching, sleep, alcohol, physical activity and cigarette smoking.

# The Lifestyle Heart Trial



**Atherosclerosis  
stenosis regression**



# The Lifestyle Heart Trial: 4 Year Extension

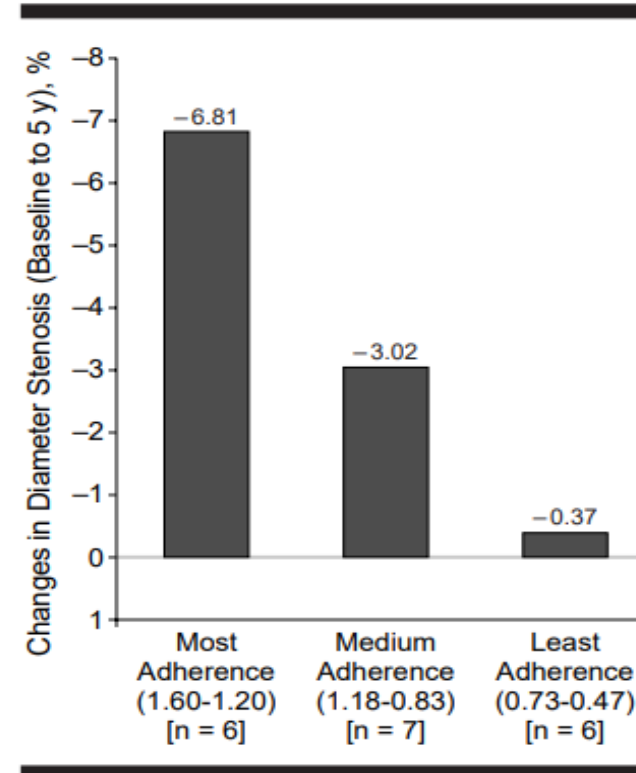
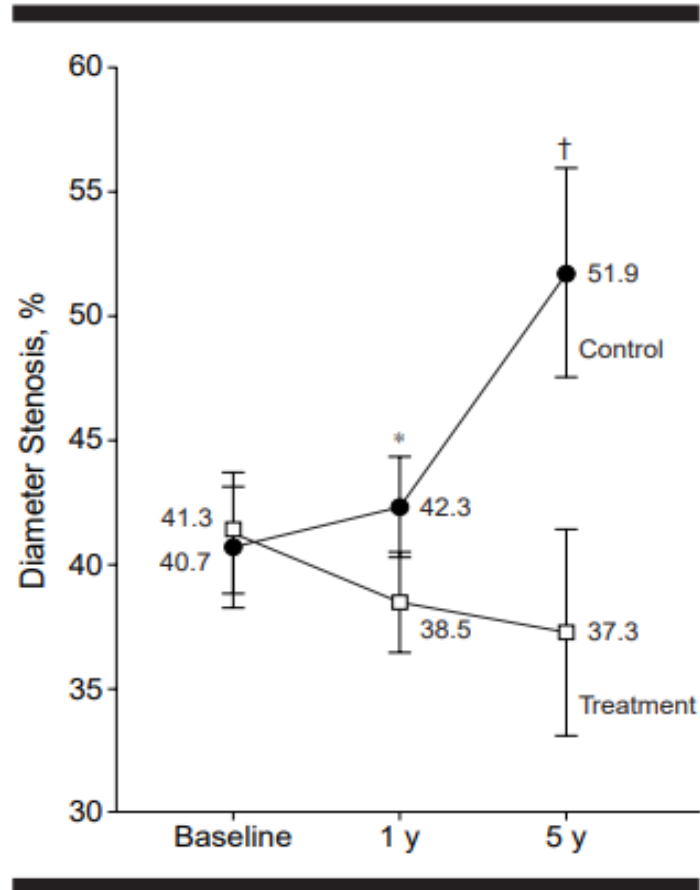


Figure 2.—Changes in percentage diameter stenosis by 5-year adherence tertiles for the experimental group.



# Cardiovascular Disease



- Cardiovascular disease (CVD) is the leading cause of death for women worldwide.
- Most CVD in women occur after 55, which is during post-menopause for most women.
- However, premature, early, or surgical menopause are also established risk factors for CVD.

North American Menopause Society, Menopause practice: a clinician's guide, Mayfield Heights, OH: The North American Menopause Society, 6th ed, 2019.

# Life's Simple 7 Predictors of Heart Health and Score



## AHA Life Simple 7 Score

1. Stop smoking
2. Eat better
3. Get active
4. Lose weight
5. Manage blood pressure
6. Control cholesterol
7. Reduce blood pressure

# Traditional vs Emerging, Nontraditional Risk Factors for Atherosclerotic CVD in Women

## Traditional

- Diabetes
- Smoking
- Obesity or excess weight
- Physical inactivity
- Hypertension
- Dyslipidemia

# Traditional vs Emerging, Nontraditional Risk Factors for Atherosclerotic CVD in Women



## Non-traditional

- Preterm delivery
- Hypertensive disorders of pregnancy
- Gestational diabetes
- Breast cancer treatment
- Autoimmune disease
- Depression

North American Menopause Society, Menopause practice: a clinician's guide, Mayfield Heights, OH: The North American Menopause Society, 6th ed, 2019.

Garcia J, et al. Cardiovascular disease in women: Clinical perspectives. Circ Res. 2016; 118(8): 1273-1293.

# Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association

<https://www.ahajournals.org/doi/10.1161/CIR.0000000000000912>



## Circulation

Volume 142, Issue 25, 22 December 2020; Pages e506-e532  
<https://doi.org/10.1161/CIR.0000000000000912>



### AHA SCIENTIFIC STATEMENT

#### Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association

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**Abstract:** Cardiovascular disease (CVD) is the leading cause of death in women, who have a notable increase in the risk for this disease after menopause and typically develop coronary heart disease several years later than men. This observation led to the hypothesis that the menopause transition (MT) contributes to the increase in coronary heart disease risk. Over the past 20 years, longitudinal studies of women traversing menopause have contributed significantly to our understanding of the relationship between the MT and CVD risk. By following women over this period, researchers have been able to disentangle chronological and ovarian aging with respect to CVD risk. These studies have documented distinct patterns of sex hormone changes, as well as adverse alterations in body composition, lipids and lipoproteins, and measures of vascular health over the MT, which can increase a woman's risk of developing CVD postmenopausally. The reported findings underline the significance of the MT as a time of accelerating CVD risk, thereby emphasizing the importance of monitoring women's health during midlife, a critical window for implementing early intervention strategies to reduce CVD risk. Notably, the 2011 American Heart Association guidelines for CVD prevention in women (the latest sex-specific guidelines to date) did not include information now available about the contribution of the MT to increased CVD in women. Therefore, there is a crucial need to discuss the contemporary literature on menopause and CVD risk with the intent of increasing awareness of the significant adverse cardiometabolic health-related changes accompanying midlife and the MT. This scientific statement provides an up-to-date synthesis of the existing data on the MT and how it relates to CVD.

# CVD Risk and Menopause Characteristics

- Age at natural menopause (non-surgically, non-chemically induced)
- Natural vs. surgical menopause or menopause type
- Stage of reproductive aging (pre, peri, post)
- Endogenous estrogens
- Hot flashes/night sweats (i.e., vasomotor symptoms)
- Problems related to sleep disturbance
- Depression
- Cardiometabolic health
- Weight gain



# Findings and Menopause Characteristics

## Age and natural menopause

- Early-onset menopause <45 are significantly at a higher risk for CVD, heart failure, and fatal CHD compared to natural menopause  $\geq 45$ , after adjusting for traditional CVD risk factors.
- Natural menopause between 50-54 compared to < 50, lower relative risk for CVD
- Some evidence to support a reverse association that later onset menopause  $\geq 55$  is related to cardiovascular mortality

# Menopause Type: Surgical Study Findings

## Bilateral Oophorectomy (BSO)

- Surgical-induced menopause caused by BSO puts women at a higher risk for CHD with no estrogen hormone therapy compared to natural menopause.
- Other studies showed BSO performed close to the age of expected menopause, showed small to no association between BSO and CHD risk, but CHD risk is higher if BSO performed < 40-45 years old.

# Stage of Reproductive Aging: Pre, Peri, Post



## Cross-sectional studies

- Women in late MT higher SBP and DBP compared to early MT

## Study of Women's Health Across the Nation (SWAN)

- Compared to premenopausal women, peri- and postmenopausal women's triglycerides, and lipoprotein (a), total cholesterol high-density lipoprotein (HDL) cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) peaked. Relative odds ratio of 2.1

Derby CA, Crawford SL, Pasternak RC, Sowers M, Sternfeld B, Matthews KA. Lipid changes during the menopause transition in relation to age and weight: the Study of Women's Health Across the Nation. *Am J Epidemiol.* 2009;169:1352–1361. doi: 10.1093/aje/kwp043

# Endogenous Estrogens



Over the MT there are alterations in endogenous hormones

Compared to a wide range of CVD risk factors, studies examining the association between estradiol and subclinical measures of atherosclerosis are more consistent.

El Khoudary SR, Santoro N, Chen HY, Tepper PG, Brooks MM, Thurston RC, Janssen I, Harlow SD, Barinas-Mitchell E, Selzer F, et al. Trajectories of estradiol and follicle-stimulating hormone over the menopause transition and early markers of atherosclerosis after menopause. *Eur J Prev Cardiol.* 2016;23:694–703. doi: 10.1177/2047487315607044

# Endogenous Estrogens

## Late Perimenopausal Women and Cross-Sectional Analyses

- Higher estradiol levels related to a smaller carotid interadventitial diameter, which suggests less carotid remodeling
- Higher estrone levels related to a higher brachial flow-mediated dilation or better endothelial function

# Endogenous Estrogens

## SWAN Studies

- Association between higher estradiol levels and lower progression of carotid inter-adventitial diameter over time
- Participants likely to develop carotid plaque if higher estradiol before their FMP but lower estradiol afterwards were less likely to develop carotid plaque, post-menopause

# Vasomotor Symptoms (Hot Flashes and Night Sweats)



Studies show that VMS during the midlife years are linked to:

- adverse lipid profile
- insulin resistance
- greater risk for incident hypertension

# Vasomotor Symptoms (Hot Flashes and Night Sweats)



Studies that compare women with and without menopause symptoms show that VMS are associated with increased risk of CVD, CHD and stroke

- Higher carotid intima-media thickness (cIMT) for women with hot flashes with higher risk for women who fall in the excess weight ranges of overweight or obese

Samargandy S, Matthews KA, Brooks MM, Barinas-Mitchell E, Magnani JW, Janssen I, Hollenberg SM, El Khoudary SR. Arterial Stiffness Accelerates Within 1 Year of the Final Menstrual Period: The SWAN Heart Study. *Arterioscler Thromb Vasc Biol.* 2020 Apr;40(4):1001-1008. doi: 10.1161/ATVBAHA.119.313622. Epub 2020 Jan 23. PMID: 31969013; PMCID: PMC7101253.



# Problems Related to Sleep Disturbance



Studies that used AHA Life's Simple 7 Scores found

- Shorter sleep duration
- Poorer sleep quality
- Greater severity of insomnia
- Associated with worse scores in postmenopausal women compared to premenopausal women

# Depression Study Findings



- Depression is related to incident CVD and VMS
- The occurrences of depression are more frequent during the perimenopausal and postmenopausal years

# Depression Study Findings



## SWAN Heart Study

Five-year follow-up in healthy women, 46–59 years old, showed that having  $\geq 3$  episodes of depression versus no episodes of depression were significantly associated with elevated coronary artery calcification scores.

Samargandy S, Matthews KA, Brooks MM, Barinas-Mitchell E, Magnani JW, Janssen I, Hollenberg SM, El Khoudary SR. Arterial Stiffness Accelerates Within 1 Year of the Final Menstrual Period: The SWAN Heart Study. *Arterioscler Thromb Vasc Biol.* 2020 Apr;40(4):1001-1008. doi: 10.1161/ATVBAHA.119.313622. Epub 2020 Jan 23. PMID: 31969013; PMCID: PMC7101253.

# Depression Study Findings



## **Women's Health Initiative (WHI trials)**

Depression was found as an independent predictor of CVD death and all-cause mortality for women with no history of CVD, after adjusting for established CVD risk factors and demographics. Follow up was an average of 4.1 years.

Wassertheil-Smoller S, Shumaker S, Ockene J, Talavera GA, Greenland P, Cochrane B, Robbins J, Aragaki A, Dunbar-Jacob J. Depression and cardiovascular sequelae in postmenopausal women: the Women's Health Initiative (WHI). *Arch Intern Med.* 2004;164:289–298. doi: 10.1001/archinte.164.3.289

# Cardiometabolic health



Longitudinal studies over the past 20 years

Over the MT:

Alterations

- In cardiometabolic and vascular health parameters linked to high CVD risk

Adverse changes in:

- Lipids
- Lipoproteins

Metabolic syndrome has been found to increase with menopause independent of age

# Weight Gain

## Changes in Fat to Lean Mass in the MT

Central and visceral fat increases and lean muscle mass decreases

The increase in central adiposity has been found to be associated with an increased risk of mortality, even for midlife women with a normal BMI

Independent of age, after menopause, paracardial fat volumes are higher after menopause, independent of age, which could be influenced by estradiol levels of MHT use

Postmenopausal women with a BMI  $\geq 40$  kg/ m<sup>2</sup>, a waist circumference of 45.35” to 48” and  $> 48$ ”, compared to waist circumference  $\leq 34.65$ ”, were found to be associated with higher total mortality and incidence of heart failure and CHD

Postmenopausal women in the normal BMI range waist circumference  $\geq 34.65$ ” were at higher risk of mortality compared to midlife women with normal BMI and no central adiposity

# Life's Simple 7 Score Does Not Include Several Areas Related to **Non-traditional ASCVD Risks** or **MT CVD Characteristics**

## Non-traditional

## MT CVD

Which of these can healthcare practitioners help to manage beyond the Life's Simple 7?

- **Preterm delivery**
- **Breast cancer treatment**
- **Autoimmune disease**
- **Depression/Depression**
- **Age at natural menopause**
- **Natural versus surgical menopause (BSO)**
- **Stage of reproductive aging (pre, peri, post)**
- **Endogenous estrogens**
- **Hot flashes/night sweats (i.e., vasomotor symptoms)**
- **Problems related to sleep disturbance**

# Age and Race Differences



## AGE

- Earlier age at natural menopause is a marker of greater risk for CVD
- Studies are inconsistent regarding race/ethnicity and timing of natural menopause, but studies have shown that Black, Hispanic, and Native Hawaiian women may experience menopause at an earlier age compared to non-Hispanic White or Japanese women



# Age and Race Differences



## **A study showed a lower percentage of knowledge about CVD with:**

- 52% of White women identifying heart disease as the leading cause of death
- 30% of Hispanic and African American women identifying heart disease as the leading cause of death

# When the At-Risk Do Not Develop Heart Failure: Understanding Positive Deviance Among Postmenopausal African-American and Hispanic Women



Journal of Cardiac Failure Vol. 27 No. 2 2021

## When the At-Risk Do Not Develop Heart Failure: Understanding Positive Deviance Among Postmenopausal African American and Hispanic Women

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### ABSTRACT

**Background:** African American and Hispanic postmenopausal women have the highest risk for heart failure compared with other races, but heart failure prevalence is lower than expected in some national cohorts. It is unknown whether psychosocial factors are associated with lower risk of incident heart failure hospitalization among high-risk postmenopausal minority women.

**Methods and Results:** Using the Women's Health Initiative Study, African American and US Hispanic women were classified as high-risk for incident heart failure hospitalization with 1 or more traditional heart failure risk factors and the highest tertile heart failure genetic risk scores. Positive psychosocial factors (optimism, social support, religion) and negative psychosocial factors (living alone, social strain, depressive symptoms) were measured using validated survey instruments at baseline. Adjusted subdistribution hazard ratios of developing heart failure hospitalization were determined with death as a competing risk. Positive deviance indicated not developing incident heart failure hospitalization with 1 or more risk factors and the highest tertile for genetic risk. Among 7986 African American women (mean follow-up of 16 years), 27.0% demonstrated positive deviance. Among high-risk African American women, optimism was associated with modestly reduced risk of heart failure hospitalization (subdistribution hazard ratio 0.94, 95% confidence interval 0.91–0.99), and social strain was associated with modestly increased risk of heart failure hospitalization (subdistribution hazard ratio 1.07, 95% confidence interval 1.02–1.12) in the initial models; however, no psychosocial factors were associated with heart failure hospitalization in fully adjusted analyses. Among 3341 Hispanic women, 25.1% demonstrated positive deviance. Among high-risk Hispanic women, living alone was associated with increased risk of heart failure hospitalization (subdistribution hazard ratio 1.97, 95% confidence interval 1.06–3.63) in unadjusted analyses; however, no psychosocial factors were associated with heart failure hospitalization in fully adjusted analyses.

**Conclusions:** Among postmenopausal African American and Hispanic women, a significant proportion remained free from heart failure hospitalization despite having the highest genetic risk profile and 1 or more traditional risk factors. No observed psychosocial factors were associated with incident heart failure hospitalization in high-risk African Americans and Hispanics. Additional investigation is needed to understand protective factors among high-risk African American and Hispanic women. (*J Cardiac Fail* 2021;27:217–223)

**Key Words:** Heart failure, racial disparities, women.

<https://pubmed.ncbi.nlm.nih.gov/33232822/>

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# Interventions

Limited RCT studies examining lifestyle interventions suggest multidimensional lifestyle interventions. Studies show that for women undergoing the MT, this type of intervention can

- Prevent weight gain while reducing:
  - Triglycerides,
  - SBP, and DBP
  - Blood glucose
  - Insulin

# Interventions

- Studies found that initiating MHT <60 years of age or within 10 years of menopause reduces the risk of CVD
- Reasonable lifestyle interventions based on current data: target ideal body weight with low central adiposity and maintenance of skeletal muscle mass.
- Diet most recommended has been the Mediterranean diet
- Lipid lowering interventions remains ambiguous



Thank you!

Questions/Discussion