Northwestern Medicine®
Feinberg School of Medicine

Heart Disease Across the Lifecourse of Women

Mercedes Carnethon, Ph.D.
Mary Harris Thompson Professor and Vice Chair of Preventive Medicine
Professor of Medicine (Pulmonary and Critical Care)
Northwestern University Feinberg School of Medicine

University of Minnesota

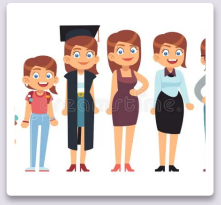
March 13, 2024

Disclosures

- No relevant support

Outline

Burden of Heart Disease among Women

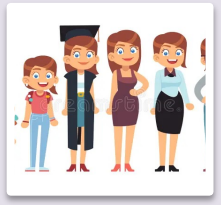


Lifecourse of Heart Disease among Women

Unique factors associated with management in women

Outline

Burden of Heart Disease among Women



Lifecourse of Heart Disease among Women

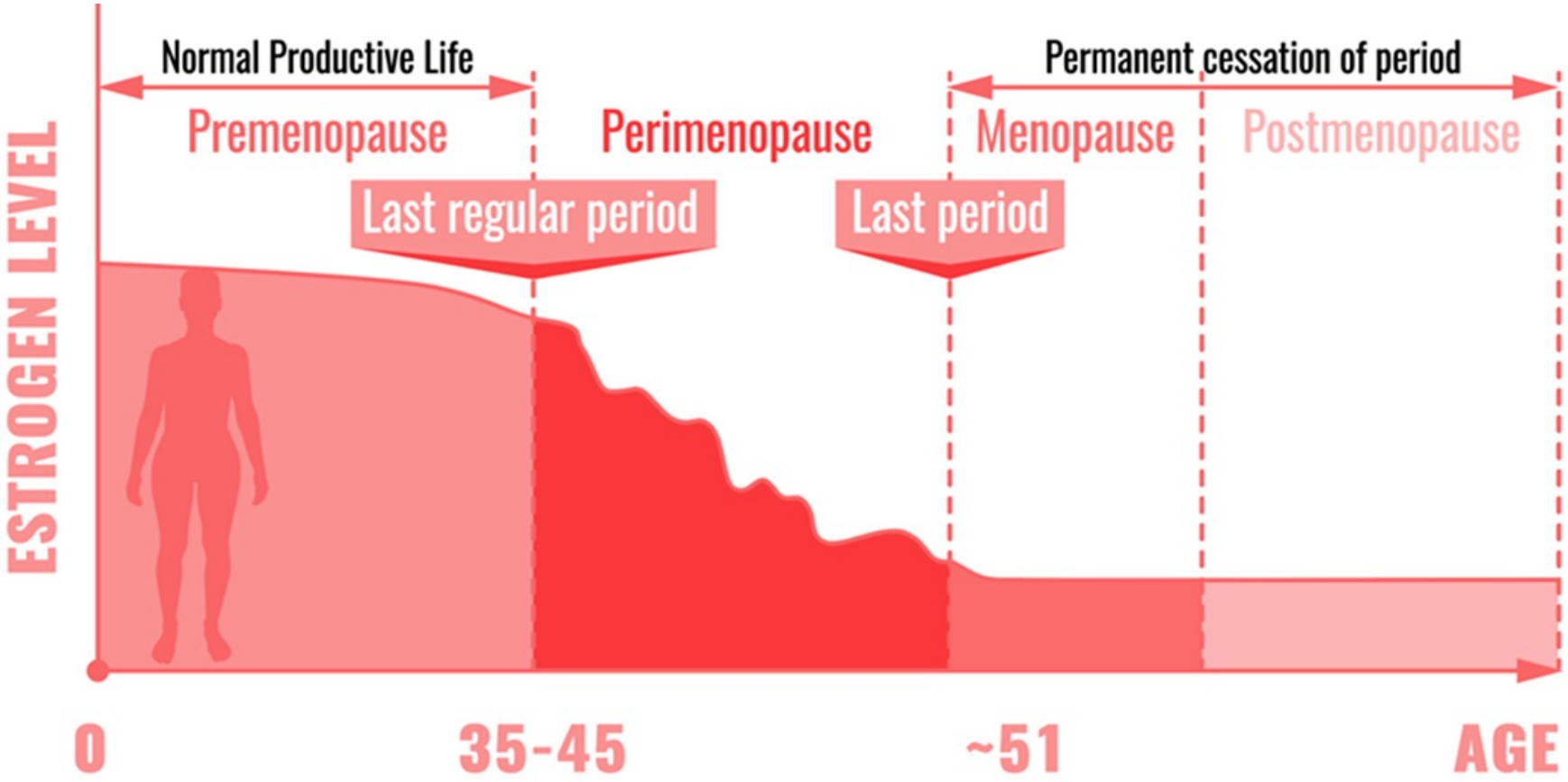
Unique factors associated with management in women

Who is a “woman”?

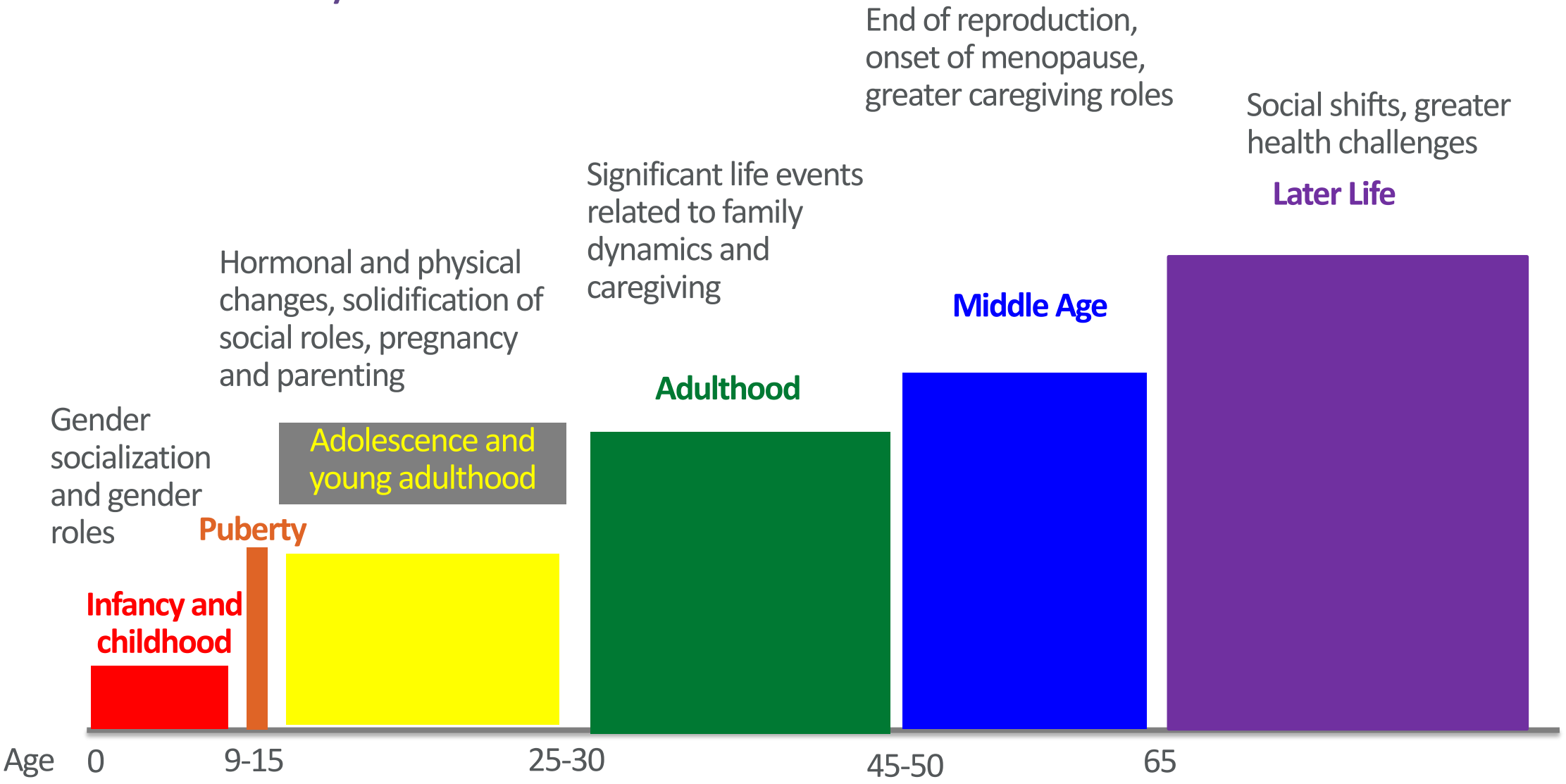
- Multidimensional
- Biological female (sex)
  - Female anatomy
- Gender identity
  - Does not need to align with sex
  - Personal identity
  - Cultural and social roles

- I will use the terminology used by the original authors in work I present
- If I am opining or summarizing, I will use the most inclusive definition of “woman” applicable to the example

Reproductive Lifecycle



Social Lifecycle of women



Intersection of the Reproductive/Biological and Social Lifecycle

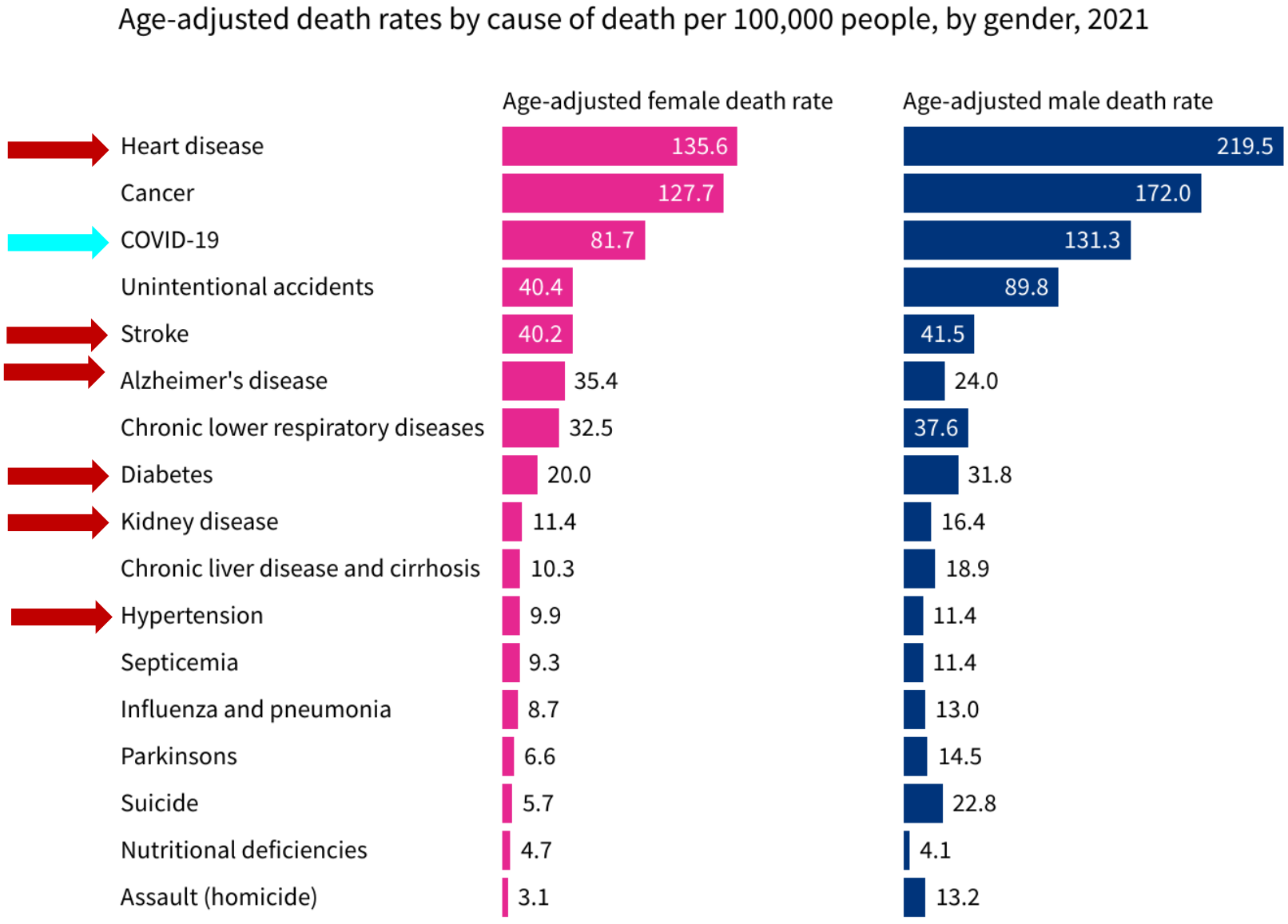
How do reproductive and social factors combine across the lifecycle to inform risks of cardiovascular disease among women?

Macrosocial cultural and social attitudes inform the behaviors of women and the ways in which the world treats women to influence cardiovascular disease risk

Facts about heart disease in women

- Cardiovascular disease (CVD) kills more women than all forms of cancer combined yet only 44% of women recognize this risk
- Nearly half (45%) of females aged>=20 years old are living with some form of cardiovascular disease
- Less than 50% of women entering pregnancy have good cardiovascular health
- Menopause itself does not cause heart disease but women's CVD risk factors can accelerate due to hormonal changes and social shifts
- A disproportionate number of deaths from stroke are among women (58%)

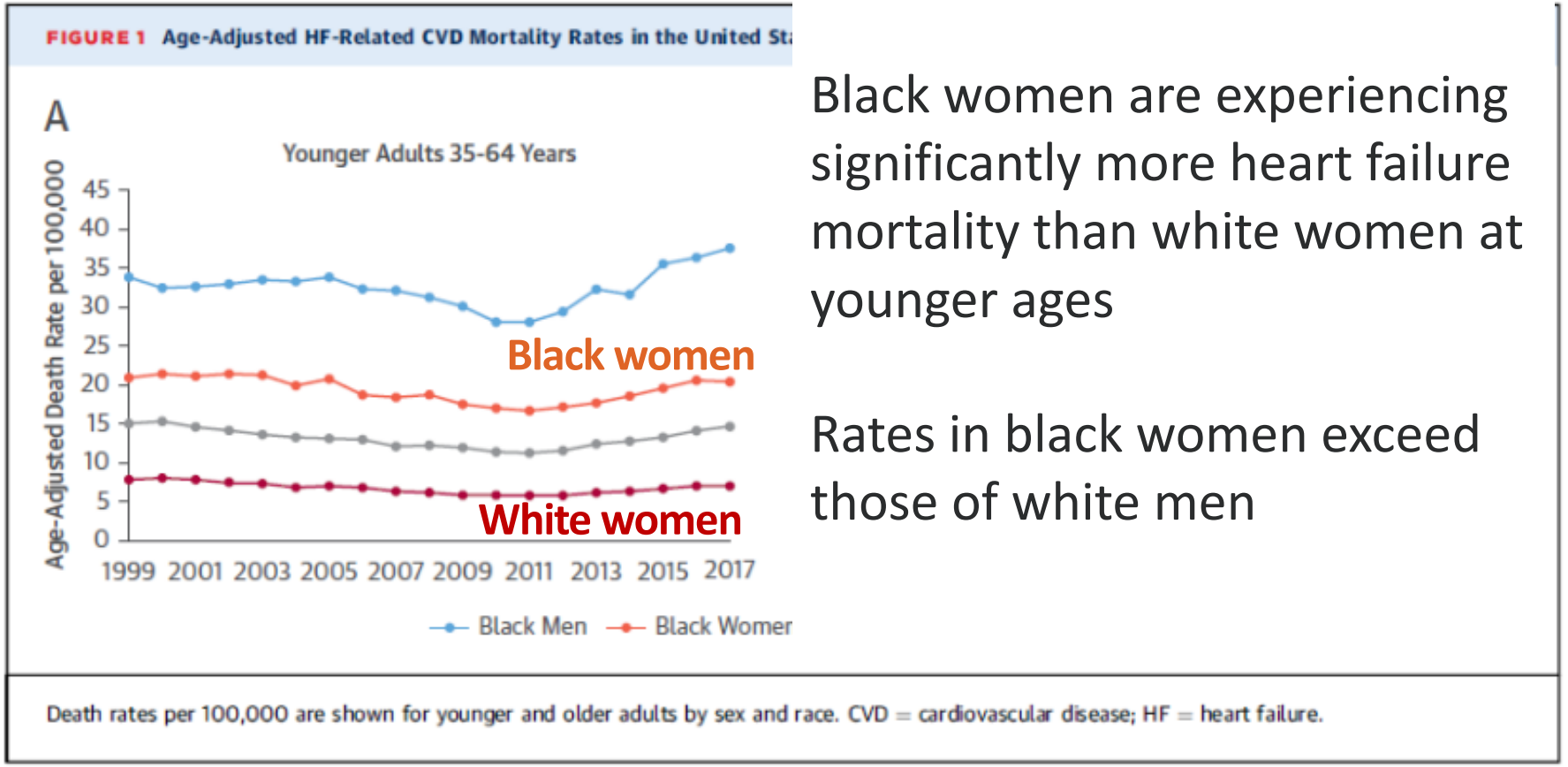
Leading Causes of Death in Females and Males in the US



Kidney disease here refers to nephritis, nephrotic syndrome and nephrosis. Stroke refers to all cerebrovascular diseases.

Source: Centers for Disease Control and Prevention

Disparities in HF-related CVD Mortality in the US



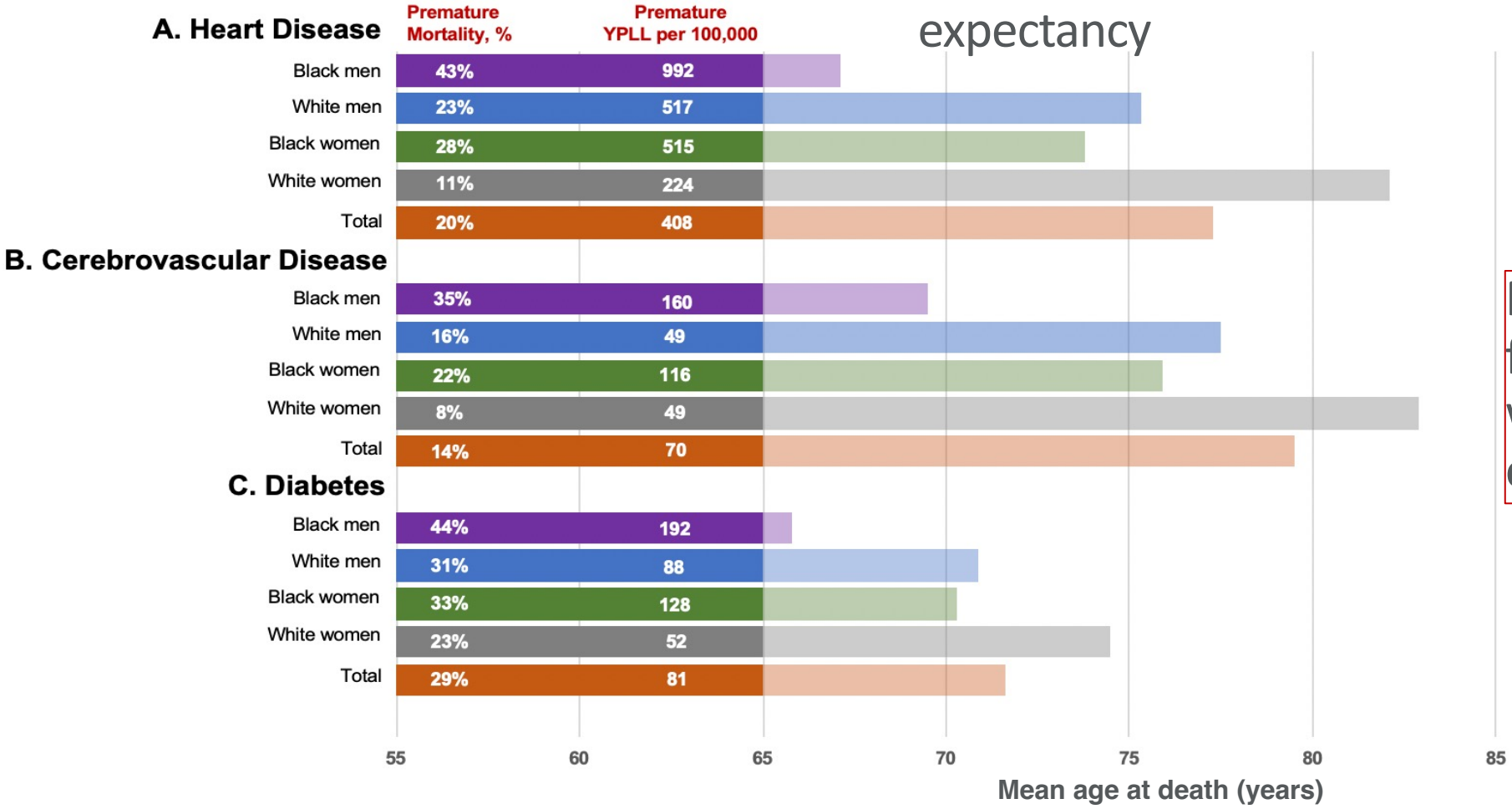
Black women are experiencing significantly more heart failure mortality than white women at younger ages

Rates in black women exceed those of white men

Glynn et al. JACC 2019; May 14; 73 (18): 2354-2355

Premature cardiometabolic disease deaths contribute to significant disparities in YPLL

Shaded bars reflect life expectancy



More years of life lost for Black and White women given longer life expectancy

Shah NS…**Khan SS**. *AHA EPI SS* 2020

Summary: Burden among women

- Cardiovascular diseases are a leading cause of death among women
  - 6 of the top 10 leading causes of death are cardiovascular, metabolic or cerebrovascular
- Early onset cardiovascular and metabolic diseases are significant contributors to years of potential life lost
- Racial disparities in cardiovascular disease are even more pronounced at younger ages among women

Outline

Burden of Heart Disease among Women

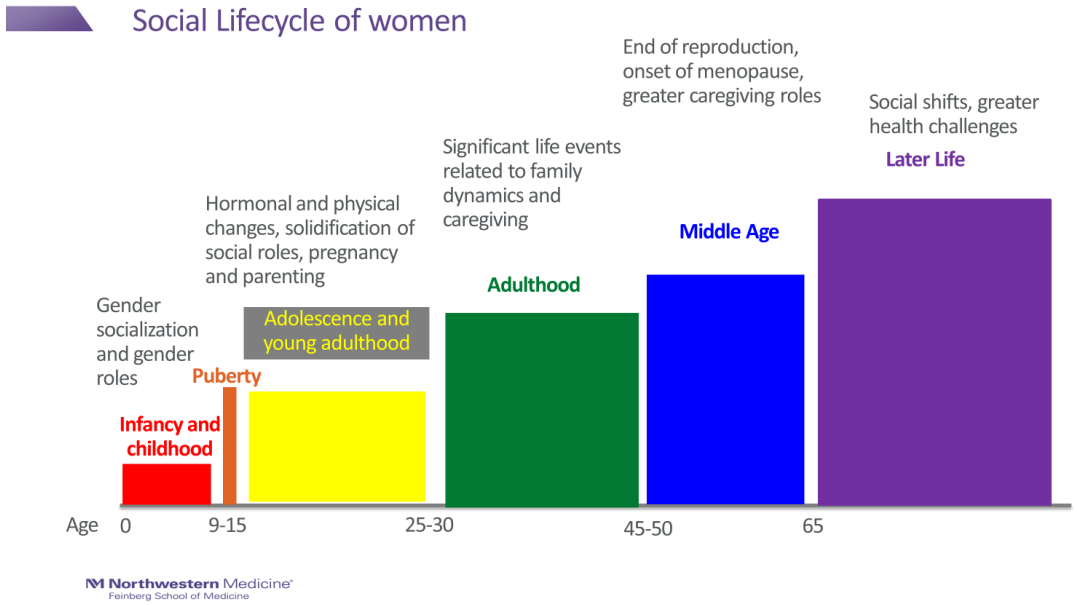
Lifecourse of Heart Disease among Women

Unique factors associated with management in women

Outline

Lifecourse of Heart Disease among Women

- Infancy and childhood
- Adolescence
- Young adulthood
- Middle adulthood
- Older adulthood

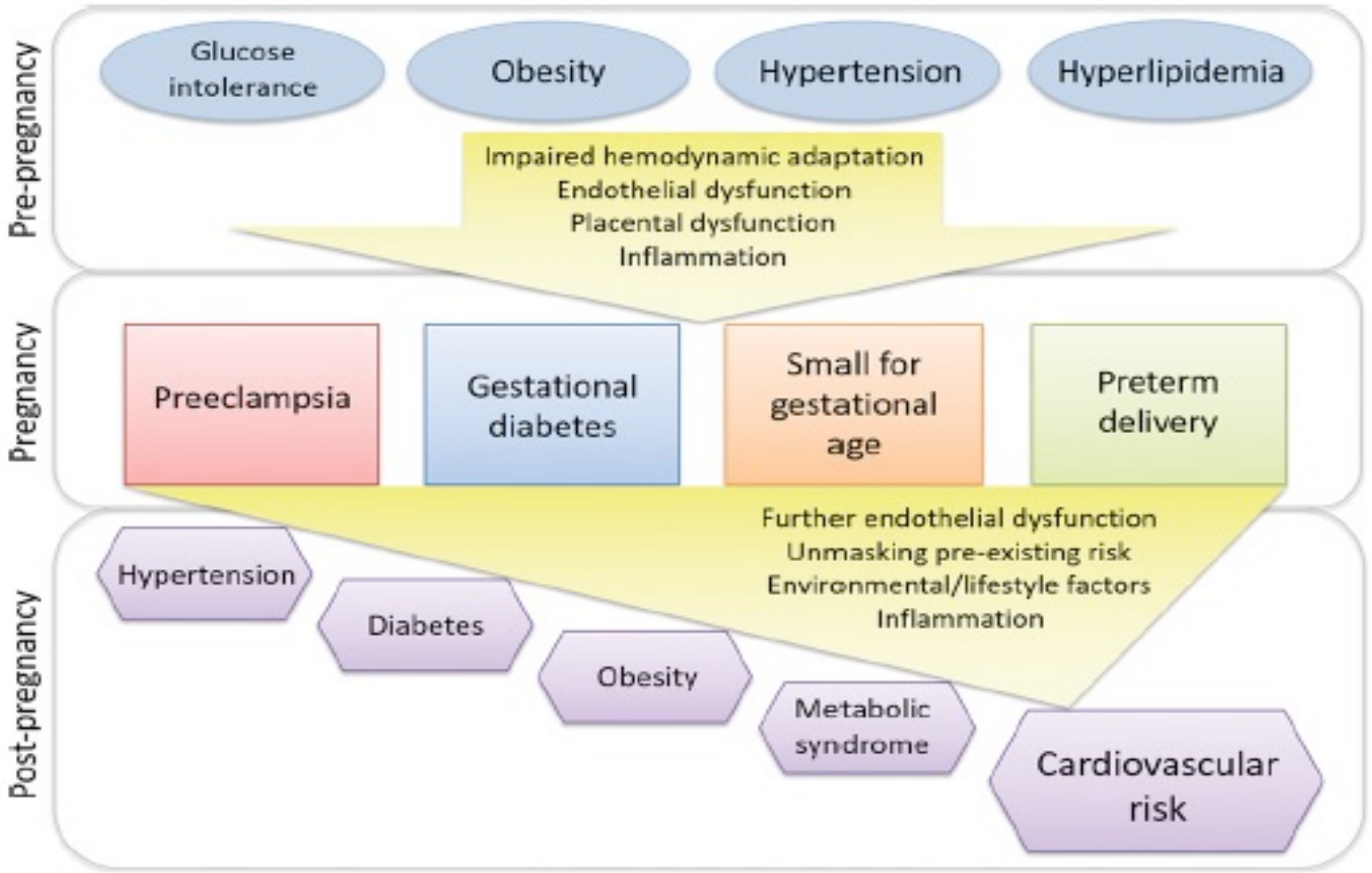


Prevalence of Adverse Pregnancy Outcomes in the US

- Collectively 10-20% of pregnancies in the US are complicated by an adverse pregnancy outcome
  - Hypertensive disorders of pregnancy affect 912 out of 10,000 deliveries
  - Pre-term birth occurred in 9.9%
  - Low birthweight in 8.2% of births
  - Significant disparities in APOs with higher rates in blacks, Latinas and low SES

- Women with less favorable cardiovascular risk characteristics going into pregnancy are at higher risk for APOs

Pre-pregnancy, Pregnancy and Post Pregnancy

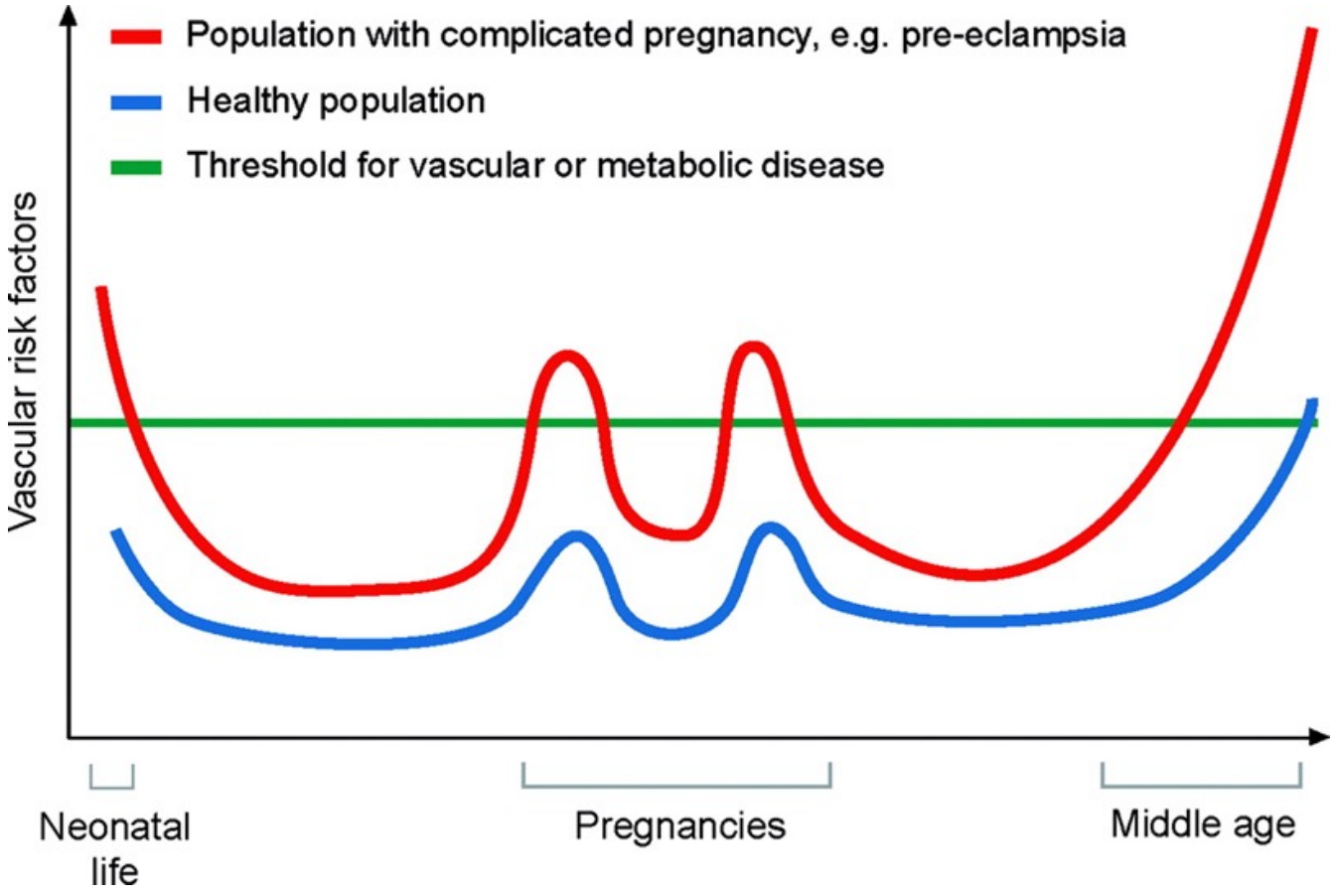


Hauspurg et al. Clinical Cardiology 2018; epub 2/15/19, DOI: 10.1002/clc.22887

Premenopausal period: Infancy and childhood

Intergenerational risk transmission of cardiovascular risk

Offspring of women who experienced APOs have a higher long-term risk of cardiovascular disease



Childhood origins of atherosclerotic cardiovascular disease

Congenital heart diseases

- Affects 1% of births (n=40,000) per year
- Growing proportion of CHD survivors are at risk for developing ASCVD with aging
- Women with congenital heart disease who become pregnant are at higher risk for APOs and deterioration of their cardiovascular function

Cardiometabolic risk factors

- Overweight and “at risk for obesity”
- High blood pressure
- Glucose disorders
- Dyslipidemia

Adverse Lifestyle Behaviors

- Physical inactivity
- Poor diet
- Sleep disturbances

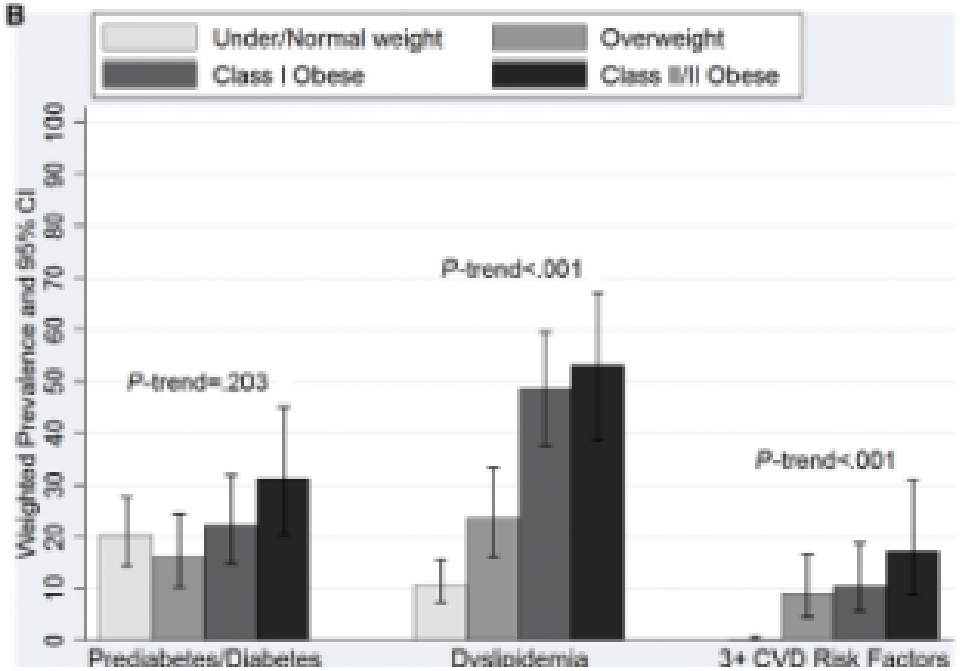
THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Sex Differences in Cardiometabolic Risk Factors among Hispanic/Latino Youth

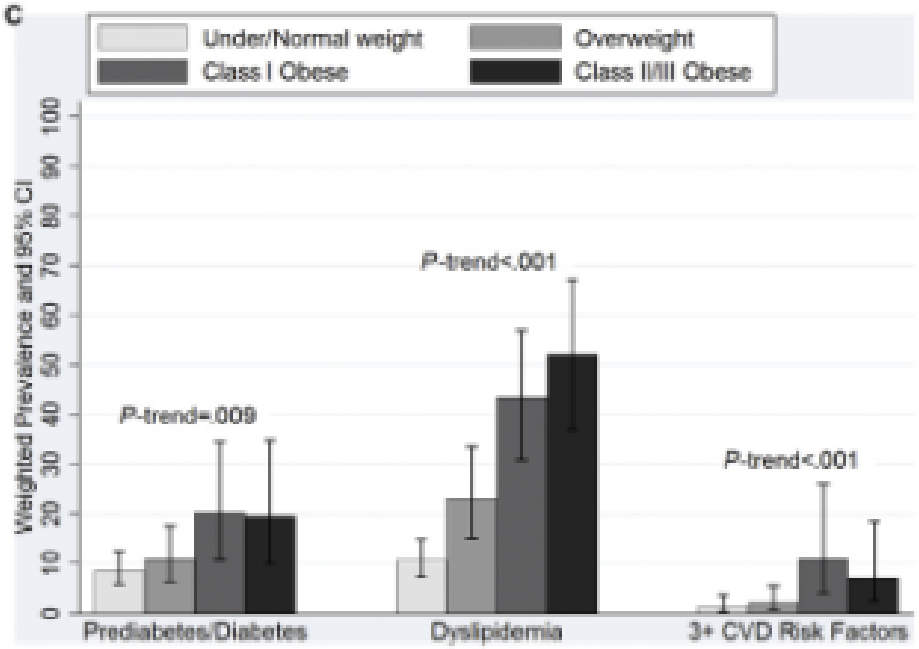
Carmen R. Isasi, MD, PhD[1], Christina M. Parrinello, PhD, MPH[1], Guadalupe X. Ayala, PhD, MPH[2], Alan M. Delamater, PhD[3], Krista M. Perreira, PhD[4], Martha L. Daviglus, MD, PhD[5], John P. Elder, PhD, MPH[6], Ashley N. Marchante, MS[7], Shrikant I. Bangdiwala, PhD[8], Linda Van Horn, PhD, RD[9], and Mercedes R. Carnethon, PhD[9]

- Cardiometabolic profiles are WORSE in boys than girls

Boys



Girls



Adolescence

- Hormonal changes during puberty
  - Social and physical effects
- Cognitive development and socialization experience rapid growth
  - Gender “Role” behavior intensifies during adolescence and a diverge emerges between girls and boys
  - Behavior changes follow changing identities
  - Interpersonal relationships outside of the family influence behavioral shifts

Physical activity declines among girls

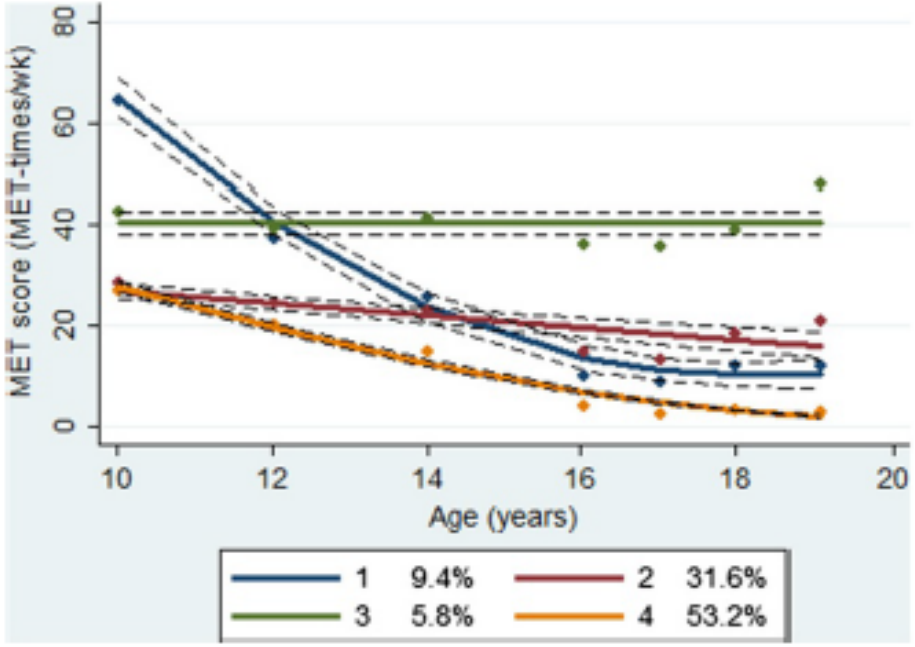
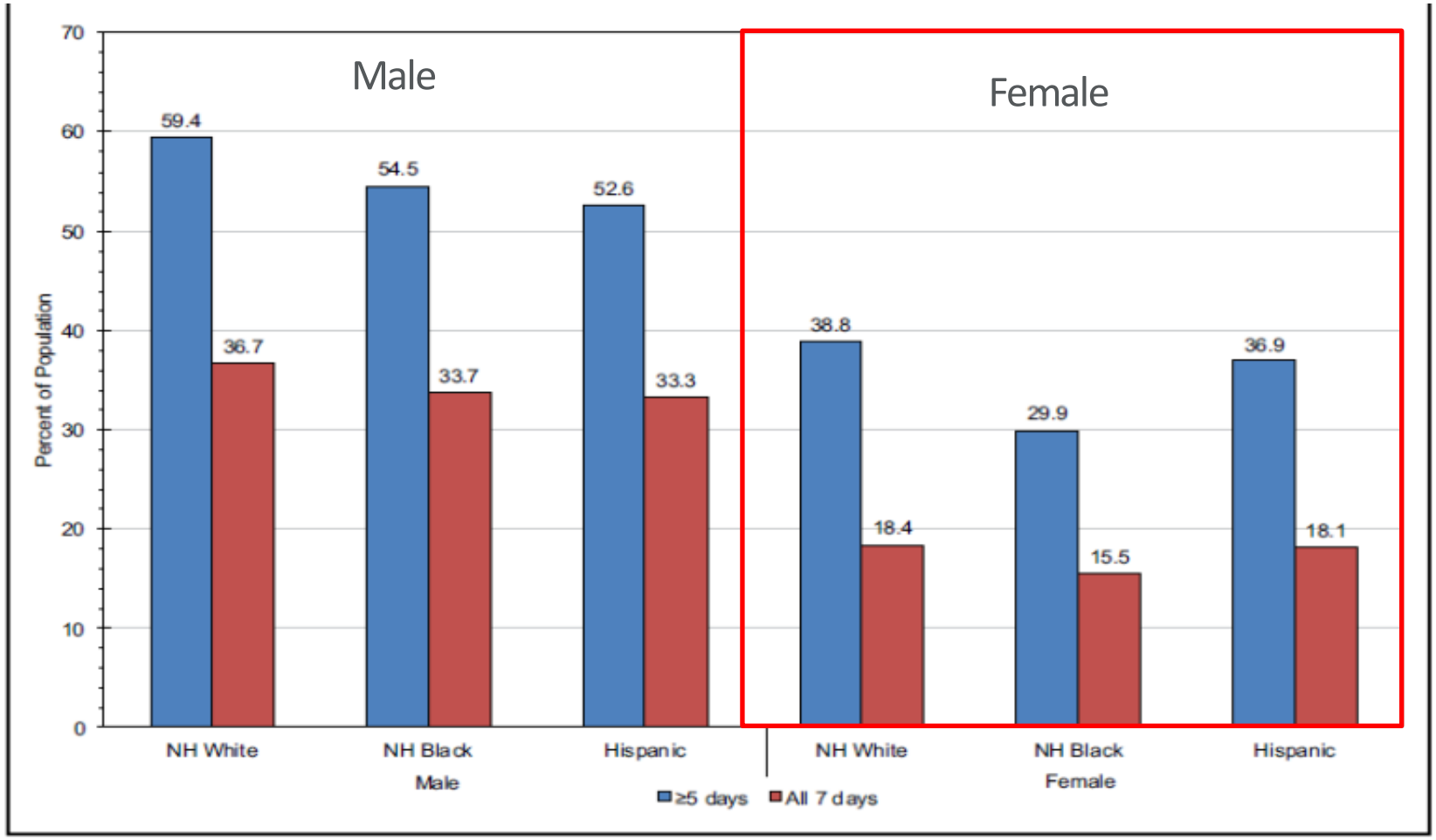


Fig. 1 Mean Habitual Activity Questionnaire scores and 95 % confidence intervals by PA trajectory classes. Dots indicate actual mean Habitual Activity Questionnaire (HAQ) scores, a solid line indicates estimated mean HAQ scores, and a dotted line indicates 95 % confidence intervals of estimated mean HAQ scores. MET, metabolic equivalent

- 4 distinct patterns of physical activity were identified over time
  - 2 groups maintained activity over time (green and red)
  - 2 groups decreased activity
- Fewer Black girls maintained activity
- Comparable data are not available for other race/ethnic groups

Kwon *et al. BMC Public Health* (2015) 15:667
DOI 10.1186/s12889-015-2043-4

Percent of US students in grades 9-12 who were active for 60 minutes/day for 7 days



Virani et al. Heart Disease and Stroke Statistics—Update 2020

Longitudinal Studies Demonstrate that Health Behaviors "Track" from Youth to Adulthood

- Few longitudinal studies measure youth as they transition into adulthood
- Consistent patterns when these data are available
  - Inactive youth and children become inactive adults
  - Diet patterns (good or bad) show relative stability
  - Youth who start out obese become more overweight or obese with time
- Pregnancy is an "inflection points" in young adulthood where behavior patterns and health risk factors worsen

70% of obese children will be obese adults

What happens after pregnancy (even in a “healthy” pregnancy)?

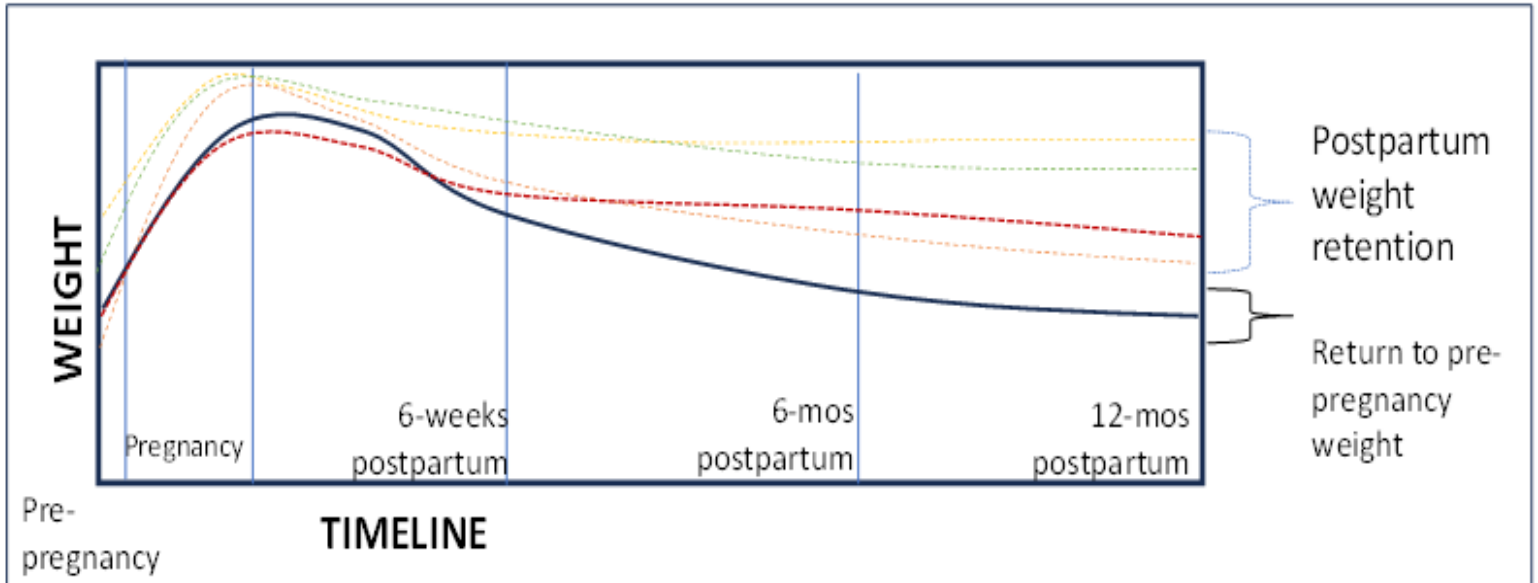


Figure B-1: Graphical Depiction of Weight During Pregnancy and Postpartum

At 1 year postpartum:

- 24% of women retain 10 lbs
- 47% retain >10 lbs
- 75% are heavier than pre-pregnancy

Endres et al. Obstetrics and Gynecology. 2015; 125: 144

Disparities in Adverse Pregnancy Outcomes

Shalon Irving, PhD

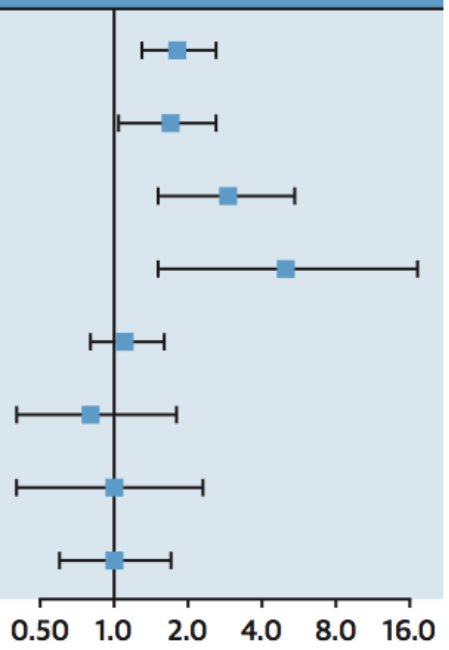
CDC Epidemiologist studying disparities

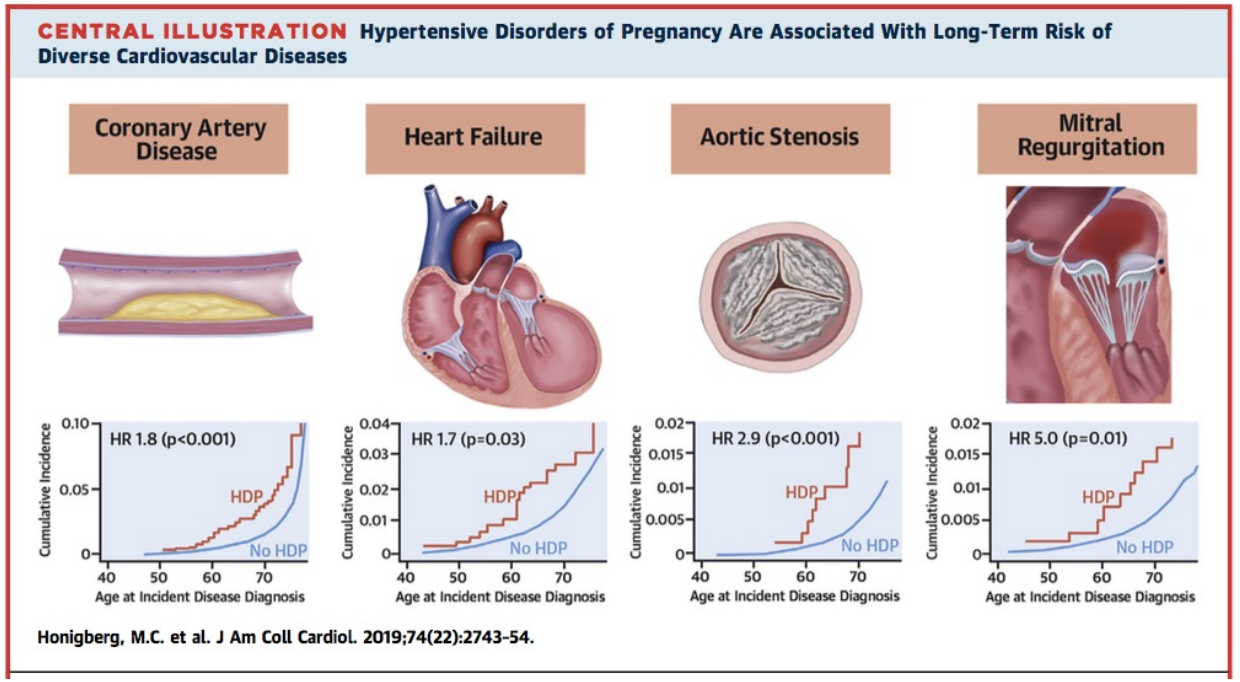
- Discharged 2 days after a c-section
- Developed a hematoma that had to be drained and had home nursing support to change the wound dressing
- Nurse noted blood pressure of 158/100 without other symptoms
- Subsequent weight gain, swelling and mild headaches
- Some time afterward, she collapsed and died

Black women are 243% more likely to die following childbirth than white women

Long-Term CVD Risk after Hypertensive Disorders of Pregnancy associated with a diversity of Cardiovascular Diseases

Cardiovascular Condition	HR	95% CI	P-Value
Coronary artery disease	1.8	1.3-2.6	<0.001
Heart failure	1.7	1.04-2.6	0.03
Aortic stenosis	2.9	1.5-5.4	<0.001
Mitral regurgitation	5.0	1.5-17.1	0.01
Atrial fibrillation	1.1	0.8-1.6	0.56
Ischemic stroke	0.8	0.4-1.8	0.57
Peripheral artery disease	1.0	0.4-2.3	0.94
Venous thromboembolism	1.0	0.6-1.7	0.97

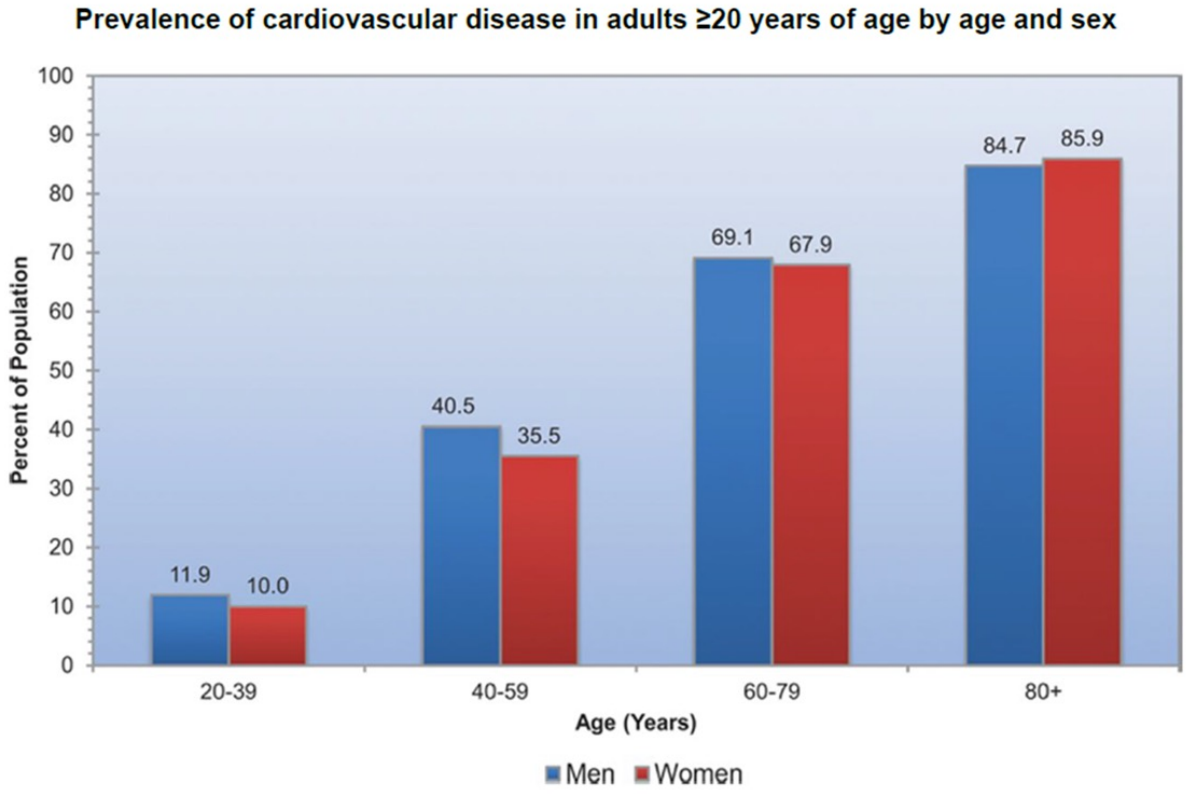




Honigberg et al. JACC. 2019;74(22):2743–54.

Sex Differences in CVD Risk During Middle- and Later- adulthood

- Higher rates in the younger two age groups but comparable prevalence in older adulthood
- Loss of protection from progesterone with the onset of perimenopause



National Health and Nutrition Examination Survey: 2009–2012.

American Heart Association.

Mozaffarian D et al. Circulation. 2015;131:e29-e322

Social Role Stress, Reward and Cardiovascular Health in Midlife Women

Findings from the Study of Women Across the Nation (SWAN)

Table 3. Relationship Between Role-Related Stress and Reward and the AHAS7 Components at SWAN From Longitudinal SWAN Data

Variable	Stress and Reward in Separate Models	
	Stress β (95% CI)	Reward β (95% CI)
No. of AHAS7 ideal components	−0.05 (−0.08 to −0.02)	0.04 (0.01 to 0.08)
AHAS7 component*	Stress OR (95% CI)	Reward OR (95% CI)
Glucose	0.89 (0.81 to 0.97)	1.06 (0.96 to 1.18)
Cholesterol	0.95 (0.88 to 1.03)	1.00 (0.92 to 1.09)
Blood pressure	0.94 (0.87 to 1.004)	0.94 (0.87 to 1.02)
BMI	0.89 (0.81 to 0.99)	1.10 (0.98 to 1.23)
Physical activity	0.83 (0.75 to 0.9)	1.38 (1.24 to 1.53)
Any healthy diet	0.92 (0.85 to 0.99)	1.05 (0.97 to 1.15)
Smoking	0.90 (0.81 to 0.99)	1.10 (0.98 to 1.23)

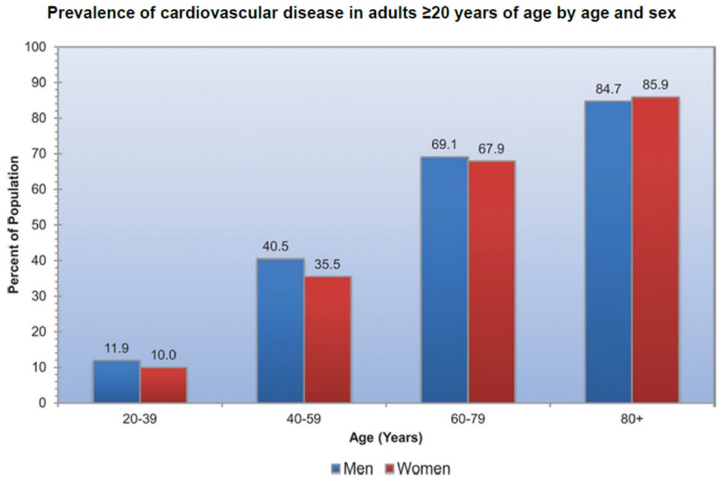
- When both stress and reward are studied simultaneously, the presence of stressors doesn't overcome the positive benefit of rewards

- Women's social role quality is associated with cardiovascular health at midlife
- Women who report greater stressful roles are less likely to achieve ideal cardiovascular health whereas women who report more rewards are more likely to report better health

J Am Heart Assoc. 2020;9:e017489. DOI: 10.1161/JAHA.120.017489

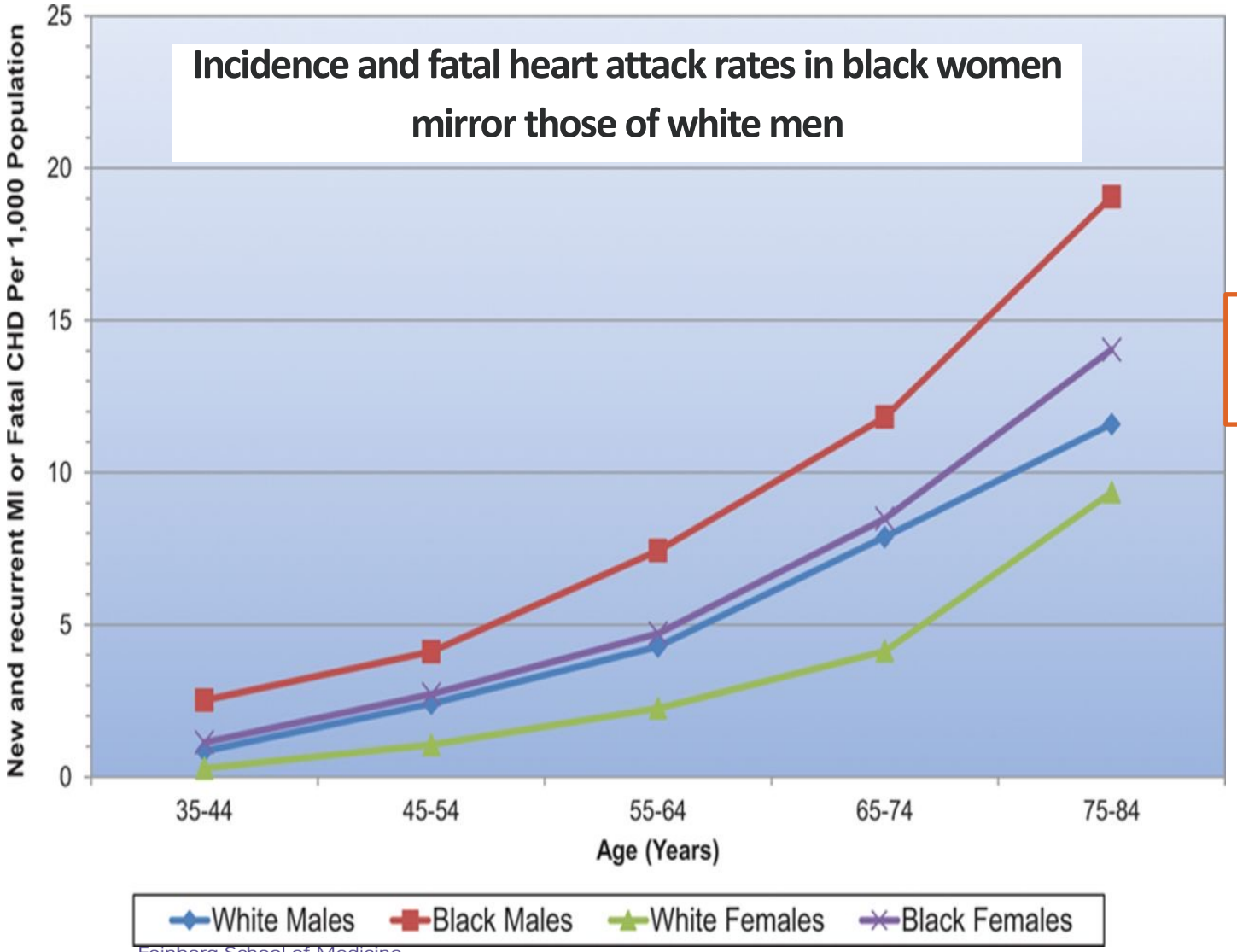
Older adulthood

- Life expectancy is longer in women as compared with men
  - Socially, more women are living alone
  - More women are caring for male partners with chronic diseases (introducing stressors)
- More women are survivors of incident cardiovascular disease
  - Enhanced risks of CVD mortality
- Higher rates of overweight and obesity among older women than older men
  - May convey higher risks for diabetes and CVD



Incidence of heart attack or fatal CHD by age, sex, and race (ARIC Surveillance: 2005–2013).

Source: National Heart, Lung, and Blood Institute



Black Males

Black Females

White Males

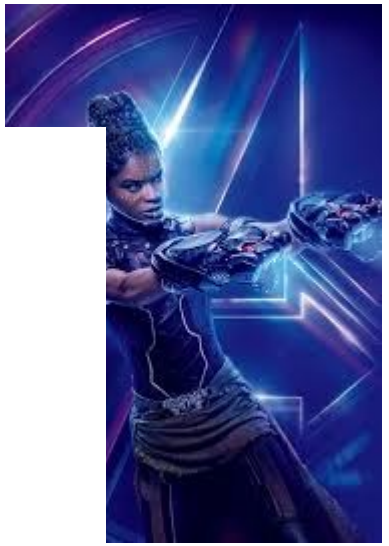
White Females

Psychosocial stressors among minority women and CV Risk Disparities

- Intersection of “sex” and “race” and the resulting “isms” can magnify the stress borne by minority women
  - Mistreatment/inadequate treatment by providers
  - Lack of access to health promoting resources

- Multiple pathways by which stress enhances cardiovascular risk
  - Adverse behavioral coping
  - Physiological stress response (e.g., sympathetic stress response, inflammation)

What is the Superwoman Schema?



Definition: A set of characteristics found in superwoman who performs or atte
associated with s
earner, mother, h

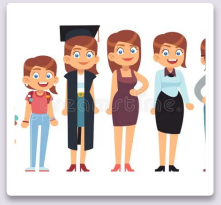
What happens w

Summary: Cardiovascular Risks Associated with Life Stages

- Cardiovascular risk in women is the culmination of a lifecourse of exposure
- Childhood behaviors track into adulthood
- Young and middle-adulthood
  - Pre-pregnancy exposures can enhance risk
  - Adverse pregnancy outcomes are associated with a diversity of cardiovascular diseases
- Older adulthood is associated with greater equality in cardiovascular risk between men and women

Outline

Burden of Heart Disease among Women



Lifecourse of Heart Disease among Women

Unique factors associated with management in women

DISCUSSION

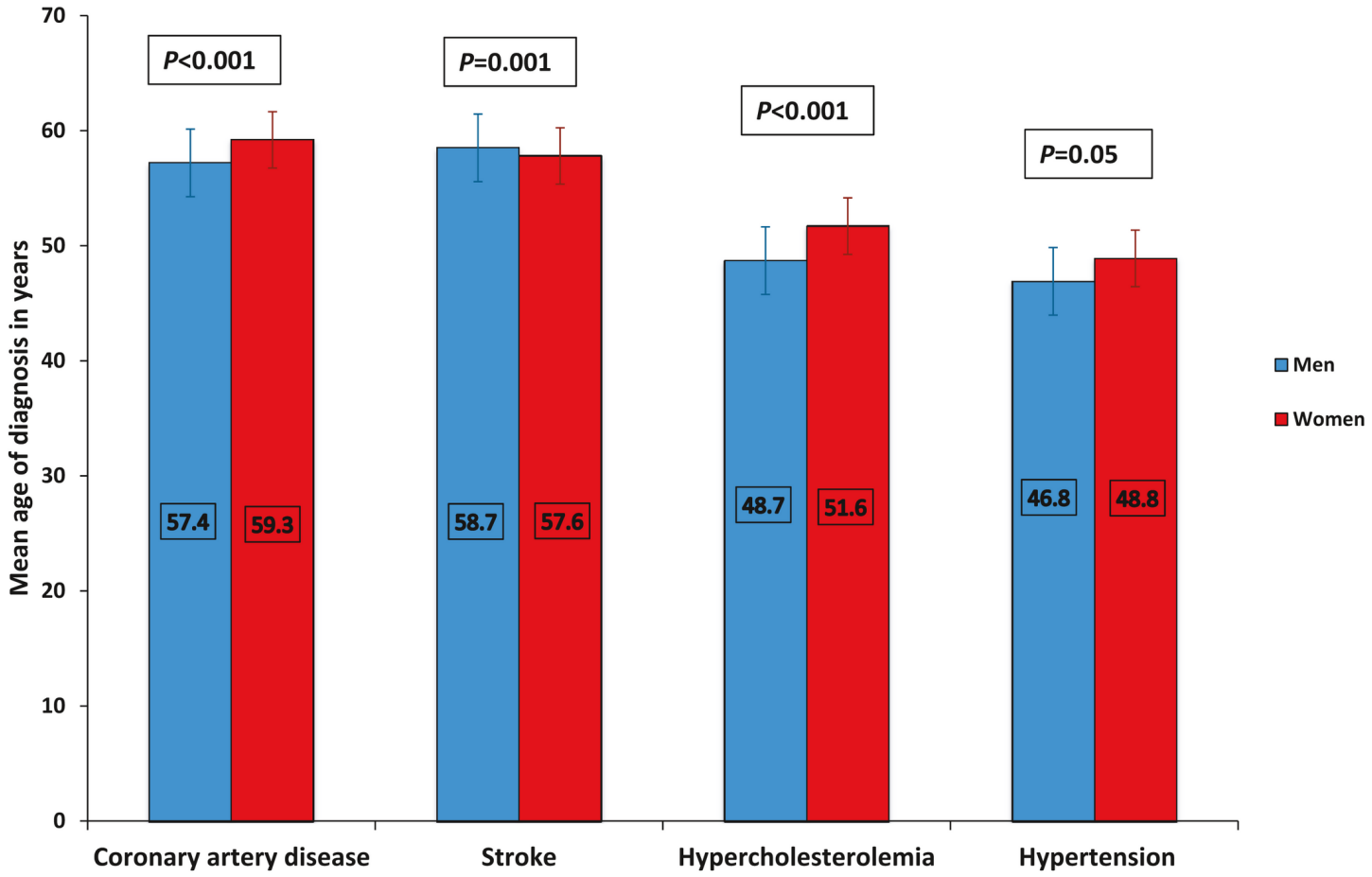
Are different preventive strategies and treatments warranted?

- If you think different strategies for management are warranted, why?
- What type of additional training is warranted in medical school to support the need for different treatments?
  - Which disciplines outside of medicine contribute to this education?

Health Services

Women are diagnosed with multiple forms of CVD later than men

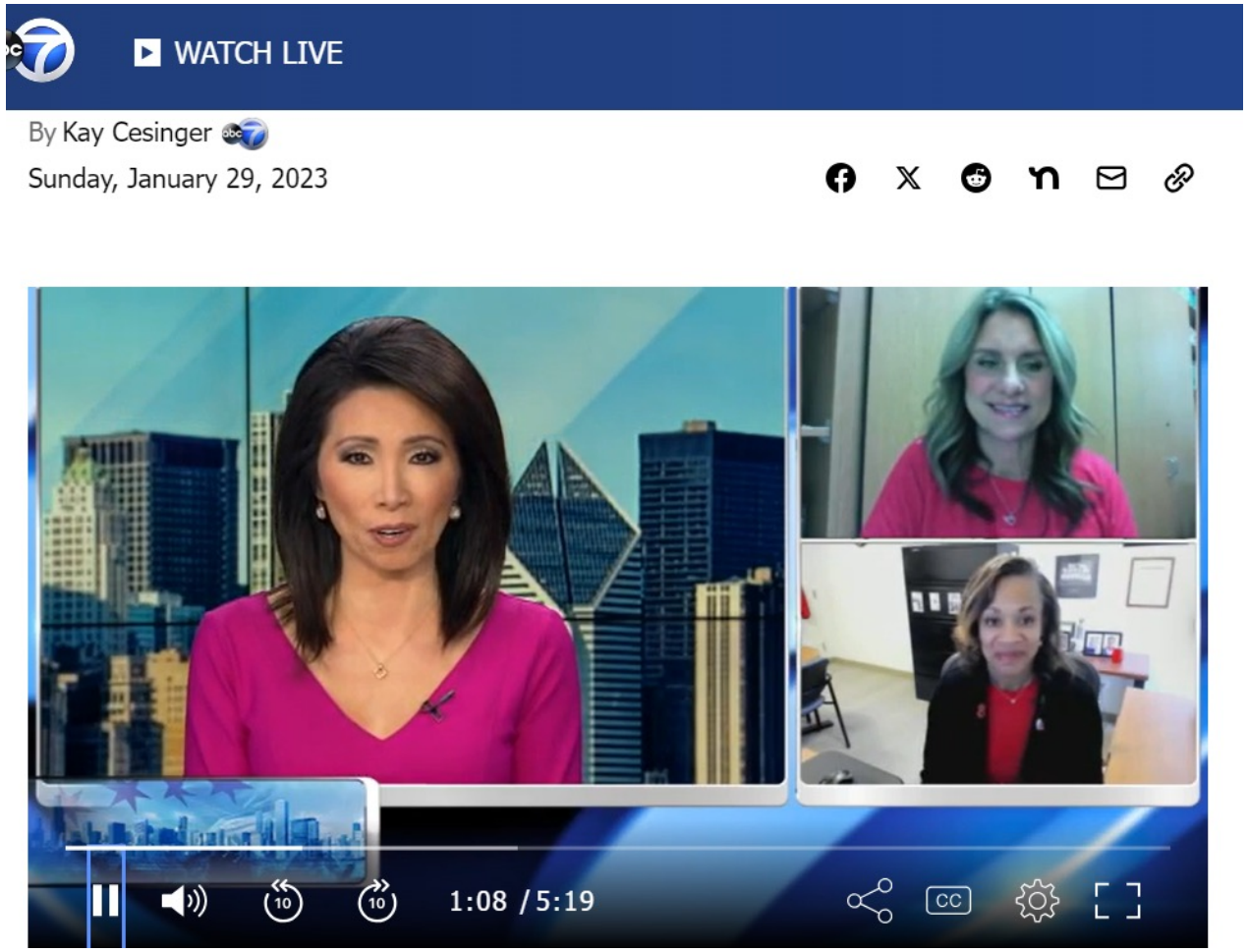
Findings from the Medicare Panel Expenditure Survey, 2008-2017



Reasons

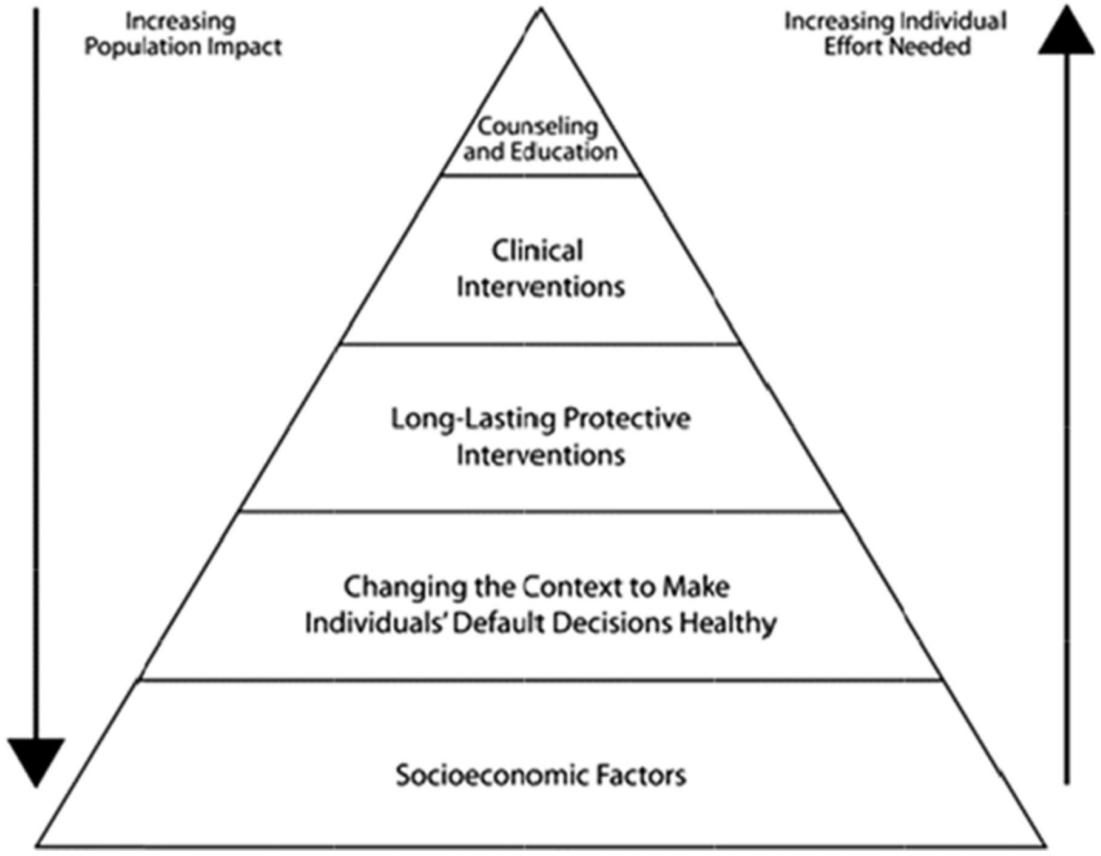
- Some of these cardiovascular diseases develop later
- Risk factors for CVD may be "different" between men and women
- Clinical presentation is different
- Women don't "look" like they are at risk for CVD

Women don’t look “at risk” and are less likely to receive bystander CPR



- In her 30s and collapsed from sudden cardiac arrest in her kitchen with her 4 kids present
- Her 15 year old learned CPR and performed it at work
- Women are less likely than men to receive bystander CPR
- Surveys cite concerns over “modesty” and touching women’s chests

Frieden's Health Impact Pyramid



- Base of the pyramid are interventions that have the broadest impact on populations
- Top of the pyramid are those that require the greatest individual effort

Pearson et al. Community Guide Circulation 2013

Summary

- Despite clear and consistent data that heart disease is a significant cause of morbidity and mortality among women, women are less often presumed to have CVD
- Medical training should emphasize that women can have a different profile of symptoms
- Training and education should support intervention when women have cardiovascular events

Thank you

- Acknowledgements to the American Heart Association
- Scientific collaborators both inside and outside of Northwestern University