



Mass General Brigham

Cardiovascular Disease in Women 2022 -A Global Crisis Presents a Golden Opportunity

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Chair ACC Board of Governors



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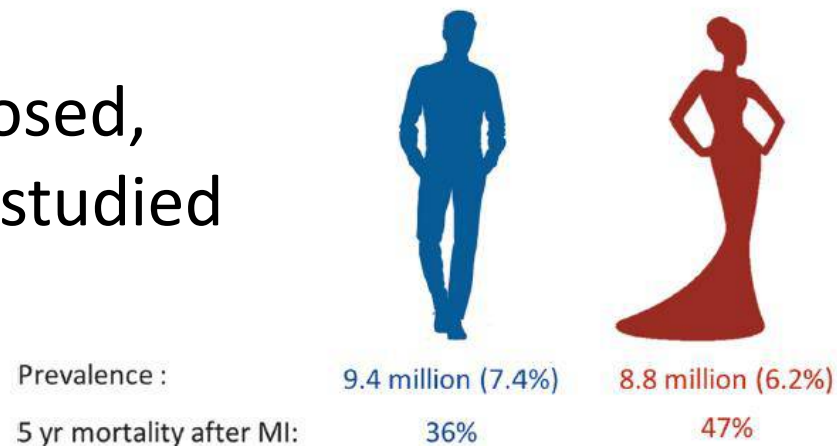


Learning Objectives



No Disclosures

- 9 million women died from CVD in 2019
- CV disease responsible for 35% of deaths in women worldwide
- Stagnation in previously favorable CVD trends
 - Women are underdiagnosed, undertreated and understudied

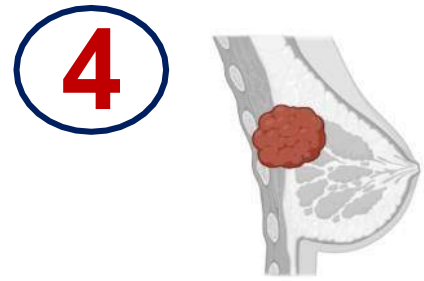
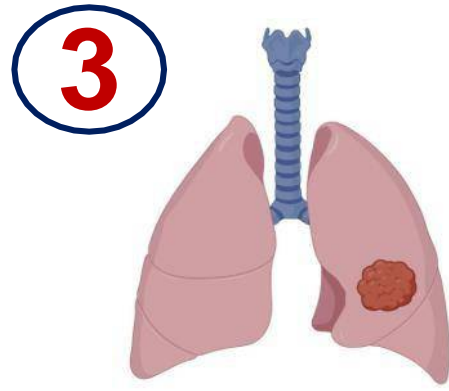
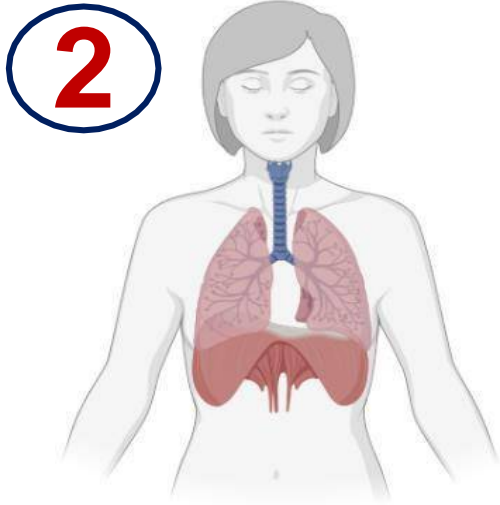
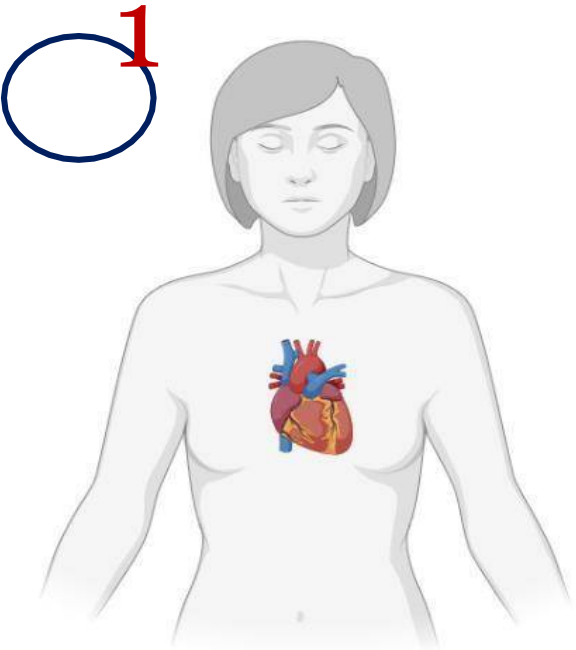


N.R. Aggarwal, M. J. Wood (Eds.) *Sex Differences in Cardiac Disease*
2021 Elsevier



1. Cardiovascular disease is the leading cause of mortality in women

Total Deaths in Women in USA 2016: 1,236,003



Cardiovascular disease 412,244 deaths	Chronic Lung Disease 81,551 deaths	Lung Cancer 70,500 deaths	Breast Cancer 40,920 deaths
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The Lancet Clinical Commission on Cardiovascular Disease in Women



The Lancet Commissions

**The *Lancet* women and cardiovascular disease Commission:
reducing the global burden by 2030**



Birgit Vogel, Monica Acevedo, Yolande Appelman, C Noel Bairey Merz, Alaide Chieffo, Gemma A Figtree, Mayra Guerrero, Vijay Kunadian, Carolyn S P Lam, Angela H E M Maas, Anastasia S Mihailidou, Agnieszka Olszanecka, Jeanne E Poole, Clara Saldarriaga, Jacqueline Saw, Liesl Zühlke, Roxana Mehran

THE LANCET



AIMS OF THE COMMISSION

1

Reduce the global burden of cardiovascular disease in women by 2030.

3

Identify existing evidence and gaps in cardiovascular research, treatment, access to care and prevention in women.

2

Promote cardiovascular health and improve outcomes for women worldwide.

4

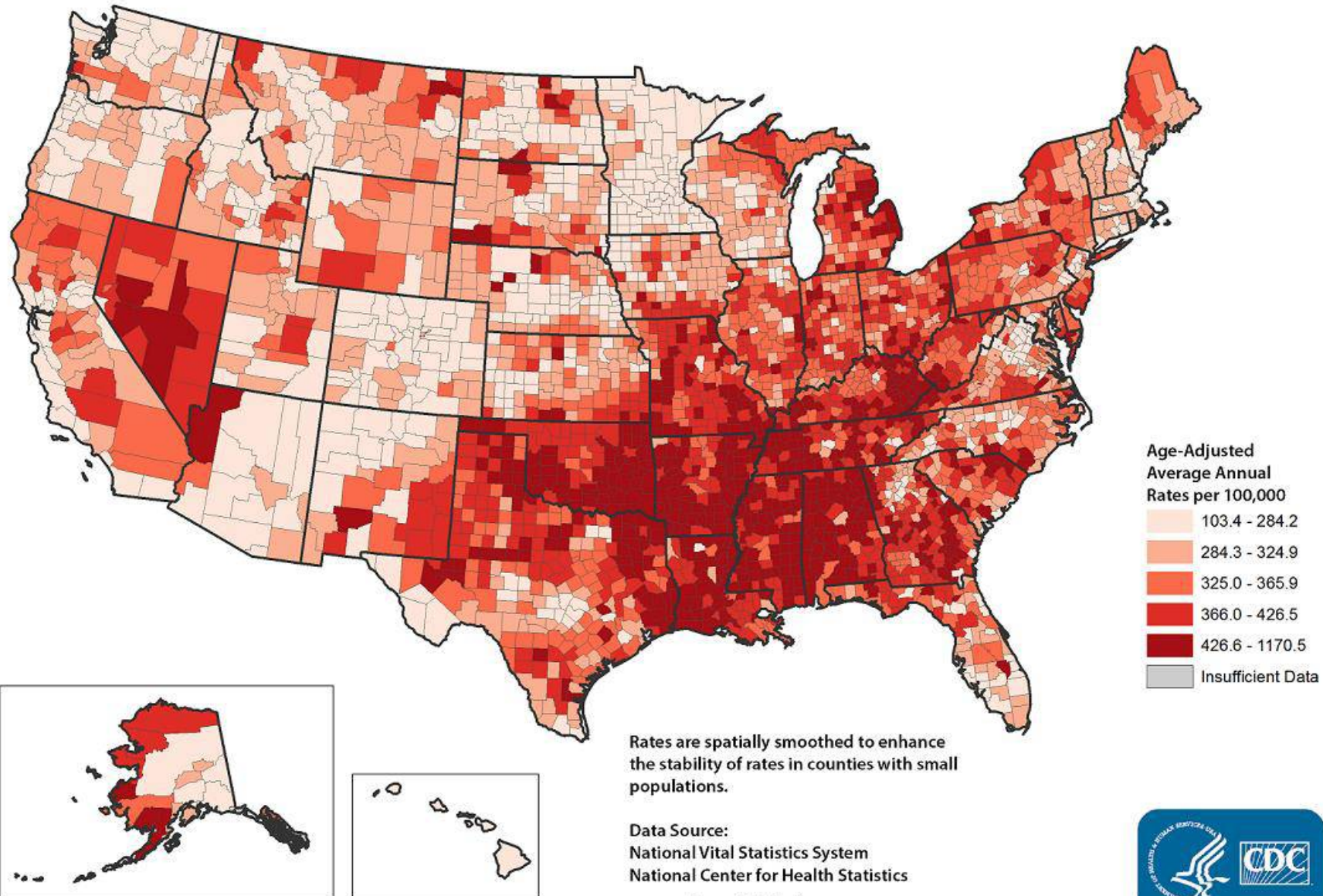
Ignite global awareness of sex- and gender-specific disparities in CVD and provide a springboard for future research.

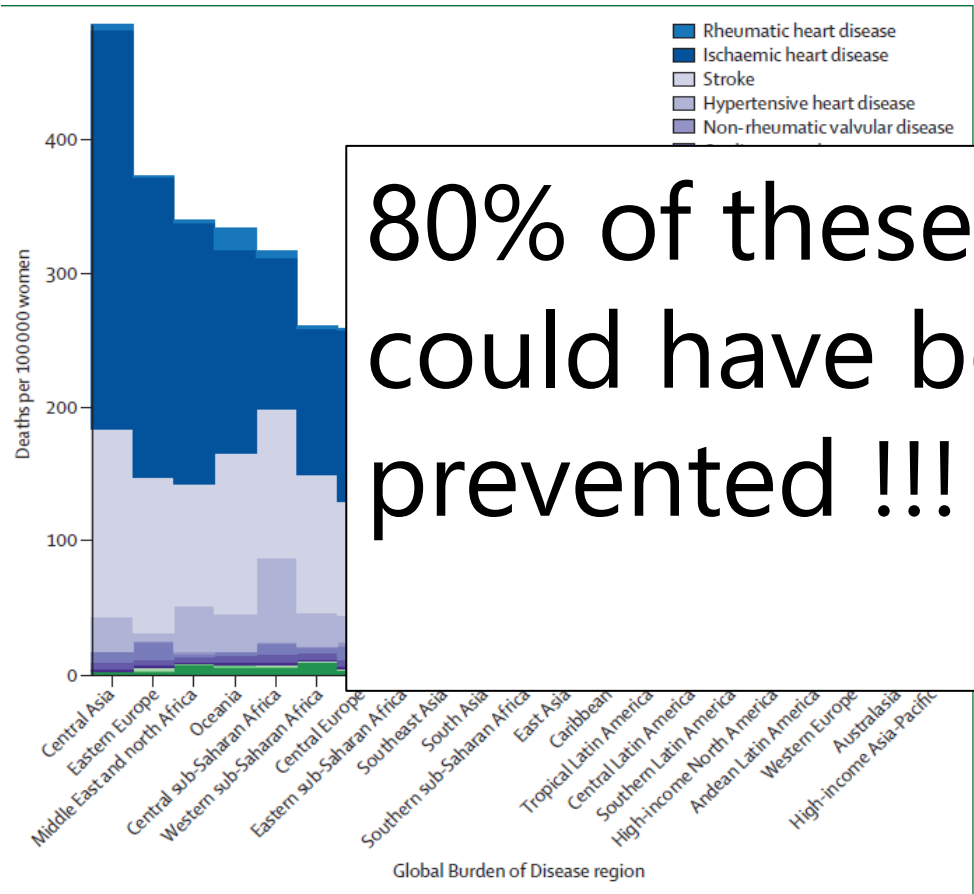


143	<u>AUSTRIA</u>	57.33
144	<u>UNITED STATES</u>	56.00
145	<u>SAINT LUCIA</u>	55.01
146	<u>SLOVENIA</u>	54.50
147	<u>BARBADOS</u>	54.40
148	<u>GERMANY</u>	54.39
149	<u>BAHAMAS</u>	53.74
150	<u>CYPRUS</u>	52.74
151	<u>COSTA RICA</u>	52.54
152	<u>ARGENTINA</u>	52.52
153	<u>GREECE</u>	50.80
154	<u>THAILAND</u>	50.49
155	<u>JAMAICA</u>	48.60
156	<u>PANAMA</u>	48.43

3	<u>NETHERLANDS</u>	31.78
4	<u>CANADA</u>	31.52
5	<u>AUSTRALIA</u>	31.02
6	<u>UNITED KINGDOM</u>	30.74
77	<u>PORTUGAL</u>	28.39
78	<u>SPAIN</u>	26.69
79	<u>DENMARK</u>	26.53
80	<u>ISRAEL</u>	26.23
181	<u>SOUTH KOREA</u>	23.16
182	<u>JAPAN</u>	21.90
183	<u>FRANCE</u>	20.58

Heart Disease Death Rates, 2014-2016 Adults, Ages 35 +, by County





80% of these deaths could have been prevented !!!

- 9 million women died from CVD

possible for in women

disease primary

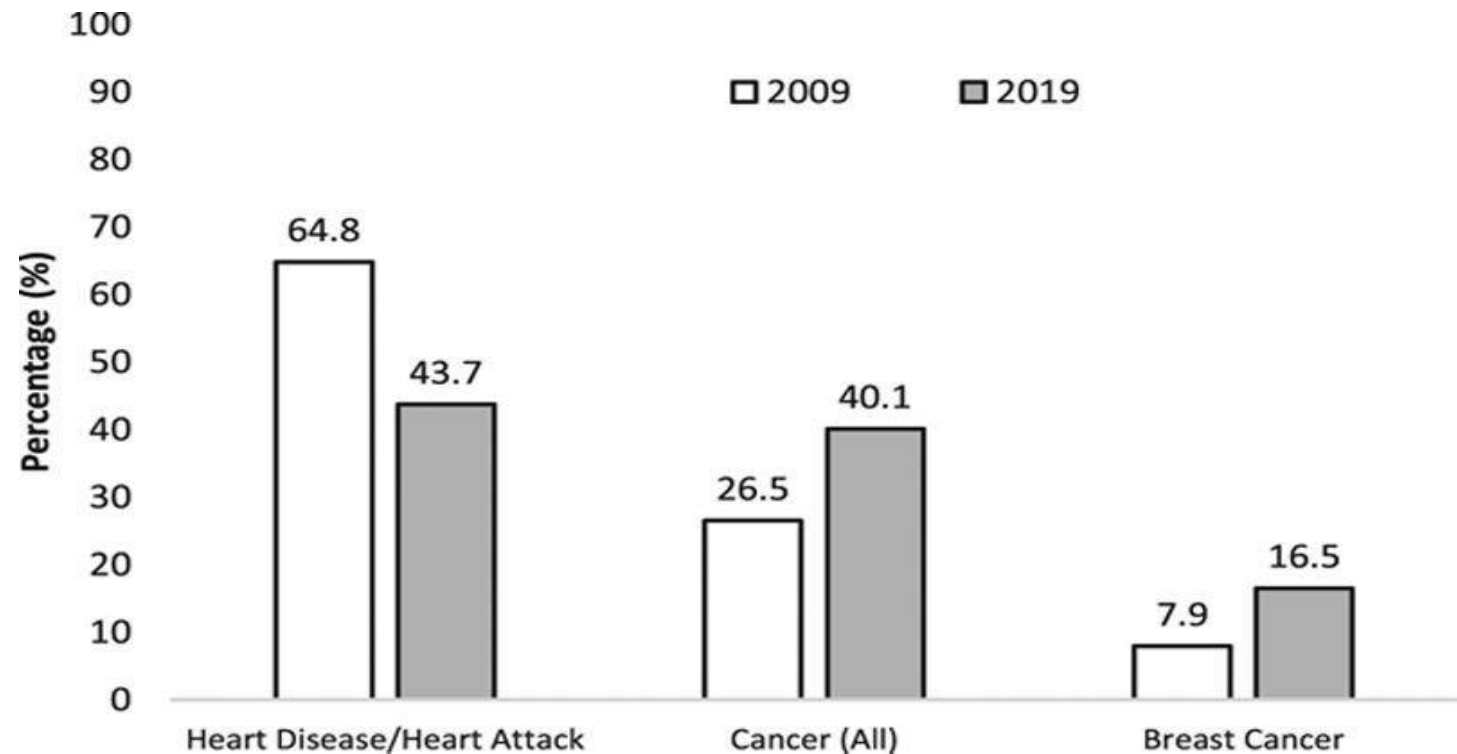
cause of CVD mortality followed by stroke

- HTN major health threat

2. Awareness that heart disease is the leading cause of death among women declined from 2009 to 2019

...particularly among Hispanic and non-Hispanic Black women and in younger women (in whom primordial/primary prevention may be most effective).

An urgent redoubling of efforts by organizations interested in women's health is required to reverse these trends.



3. Women are still underrepresented in cardiovascular clinical trials

Though legislation passed in the 1980s and 1990s mandated the inclusion of women in clinical trials:

Selected Major CV Device Trials			
Year	Device Type	Trial	% Women
2008	CRT-D	REVERSE	21
2009	CRT-D	MADIT-CRT	26
2008	Coronary Stent	SPIRIT III	31
2015	Coronary Stent	BEST (Asian Trial)	29
2012	LVAD	HMII DT	21
2014	LAAO	PREVAIL	30

Women are
UNDER-REPRESENTED

in clinical trial
participation

representation

THE TRIAL

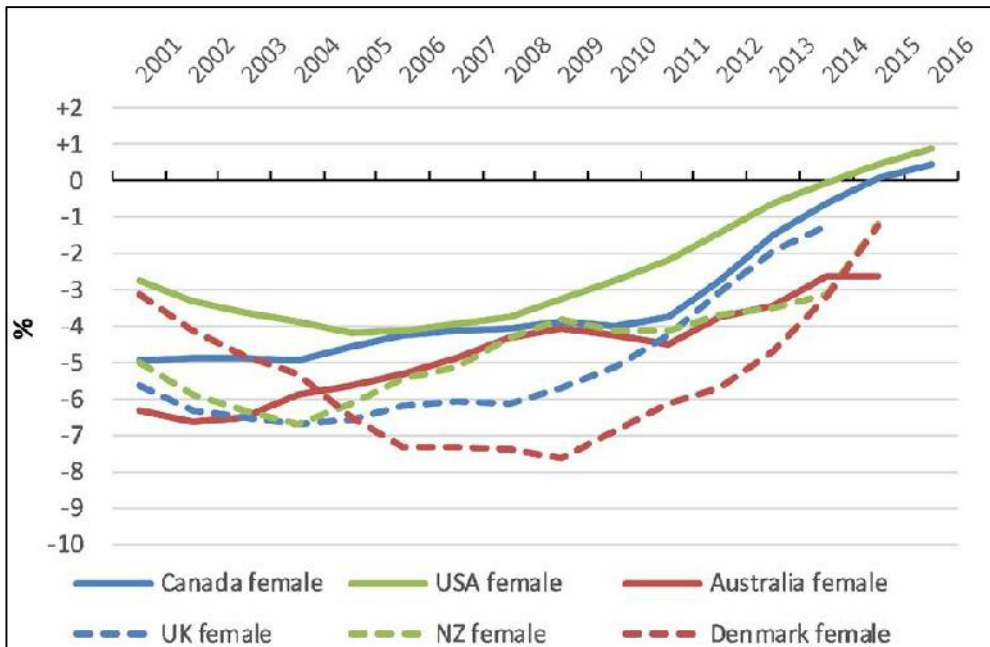
sex-specific
recommendations
for disease in

women

2017

Participation prevalence ratios were 0.48–0.78 for trials in heart failure, acute coronary syndrome, coronary heart disease, stroke, and arrhythmia (PPR of <0.8 indicates underrepresentation in relation to disease prevalence). PPR = measure to describe the representation of women in trial with respect to their proportion in disease population

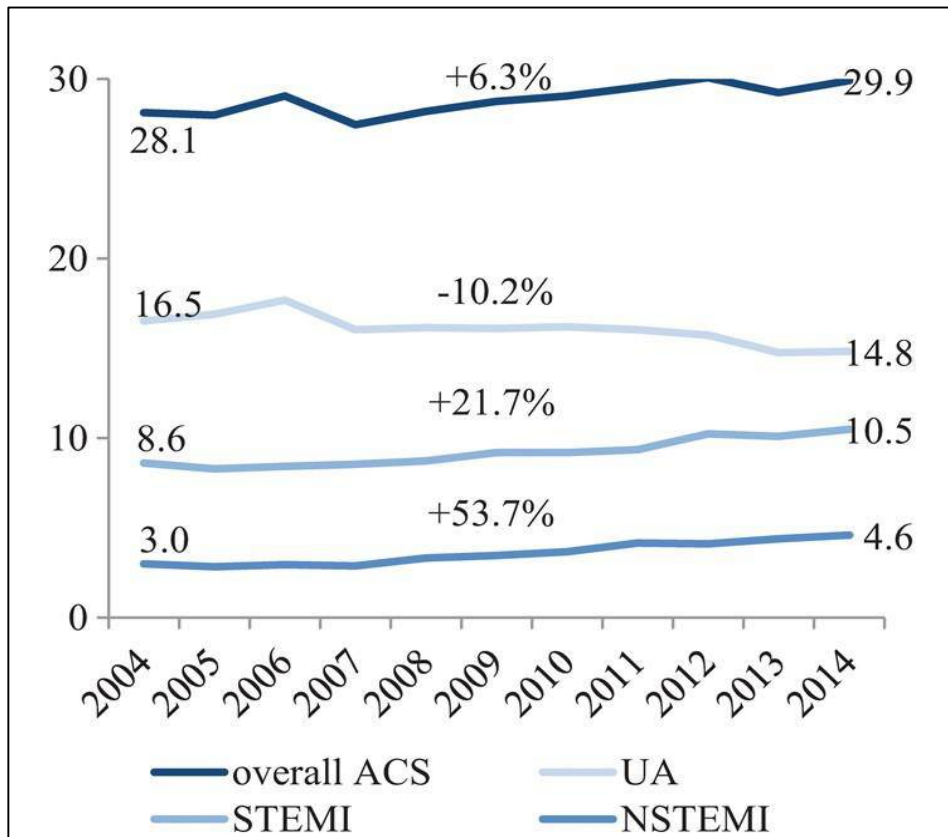
4. In high-income regions, the decline in CVD mortality has slowed and CVD mortality has increased in women from certain countries



An analysis of the WHO Mortality Database found an increase of age-standardized cardiovascular disease death (35–74 years) during recent years in women in the USA and Canada.

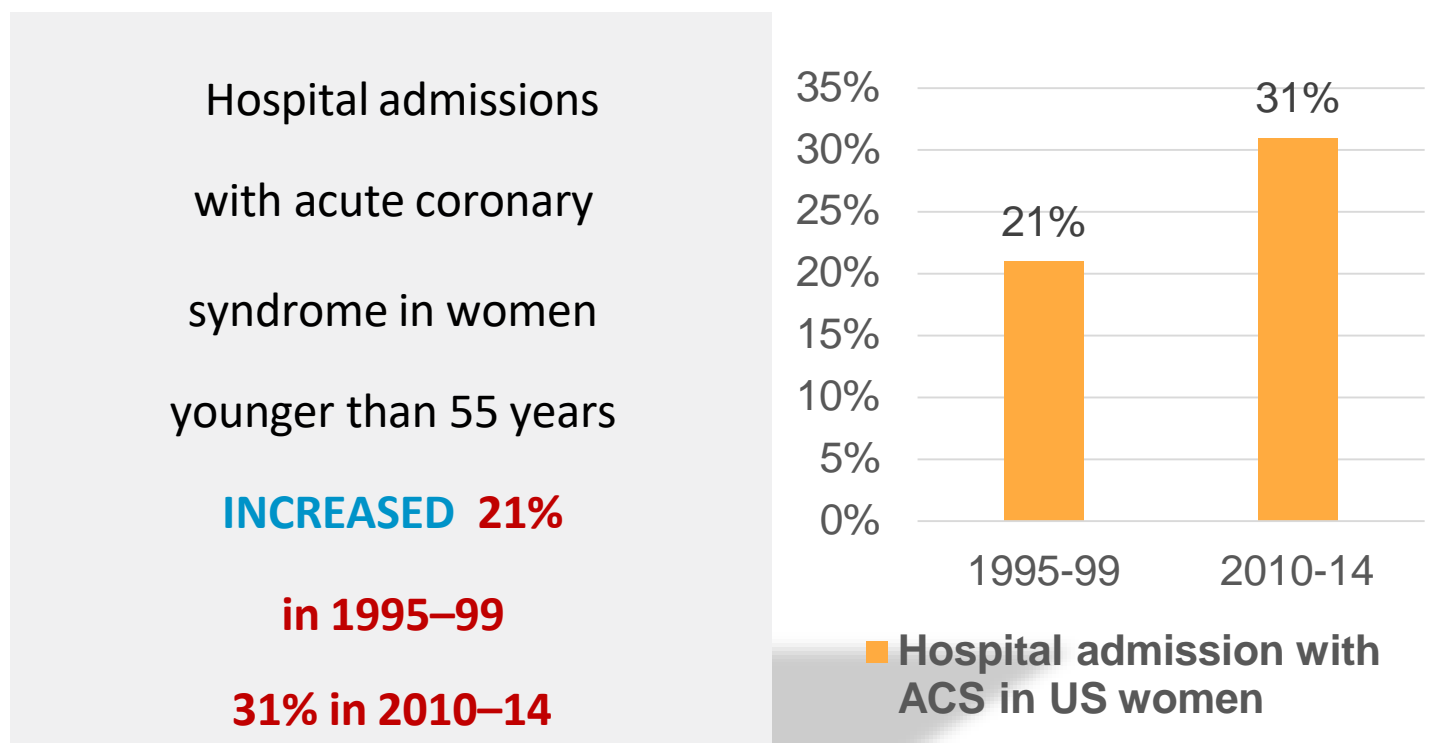
5. There is an increase in myocardial infarction in young women

French women <65 years of age



Gabet A et al., Eur Heart J 2017

Data from US



Arora S et al., Circulation 2019

Sex Differences in Management of Acute MI- YOUNG MI Study

2097 individuals with MI at age ≤ 50

Women = 404 (19%)



Men = 1693 (81%)



Risk Factors

- Women were more likely to have diabetes and underlying rheumatic conditions
- Women had lower median income and more likely to have public insurance

Clinical Presentation

- The most common presenting symptom in both women and men was chest pain
- Women were more likely to also have dyspnea, palpitations, or fatigue

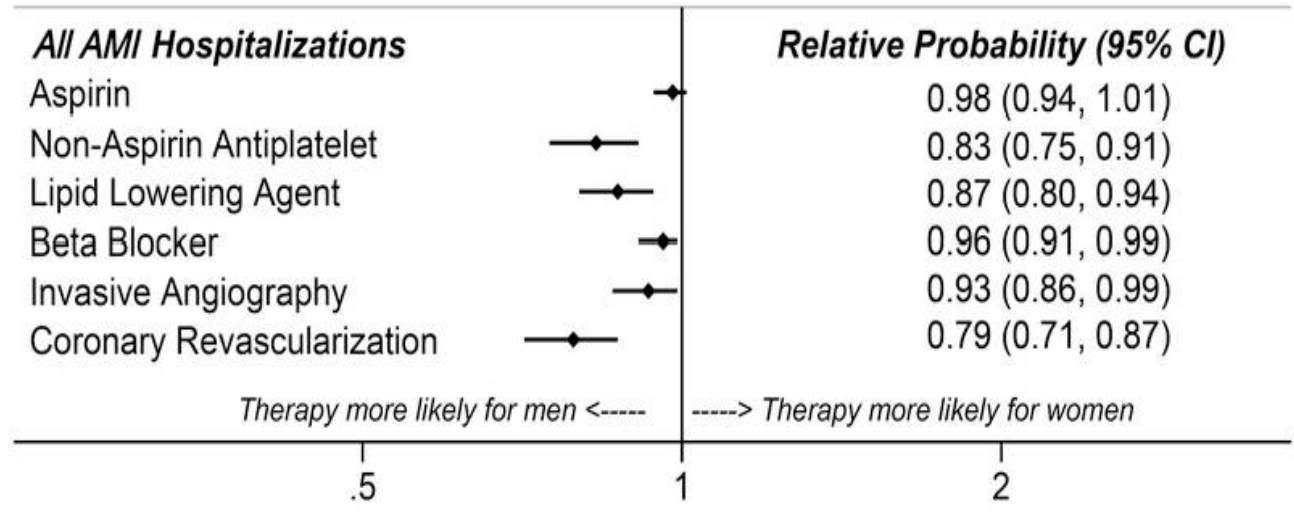
Management

- Women were less likely to undergo angiography and revascularization
- Women were less likely to be on guideline-directed post-MI medications

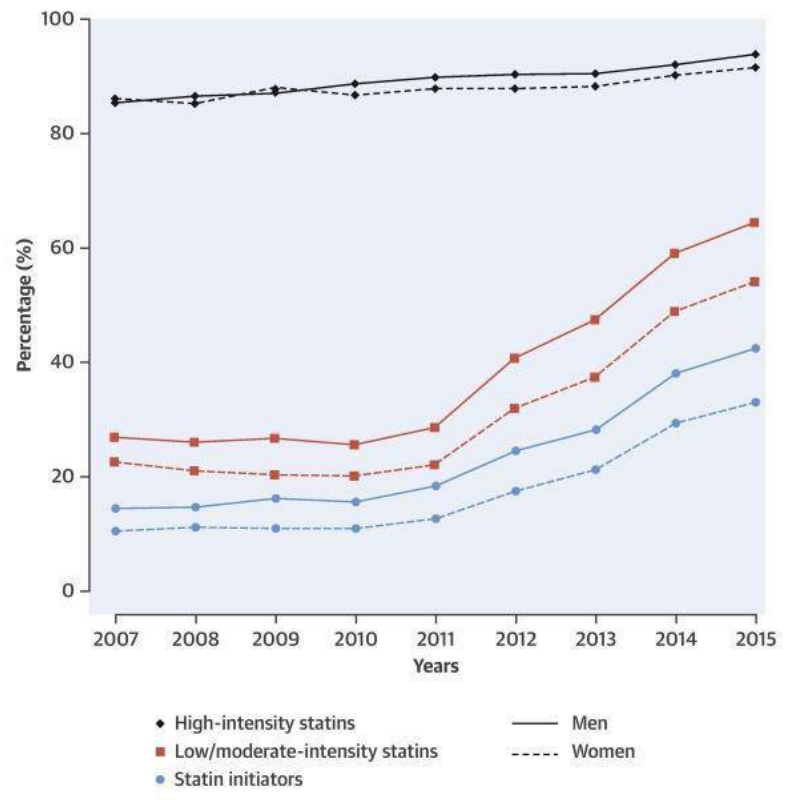
Outcomes

- Women had increased all-cause mortality over a median follow-up of 11.2 years

Patients with myocardial infarction:




CENTRAL ILLUSTRATION: Trends in the Percentage of Women and Men Filling a High-Intensity Statin Prescription After Hospital Discharge for Myocardial Infarction Between 2007 and 2015



Peters, S.A.E. et al. J Am Coll Cardiol. 2018;71(16):1729-37.


6. Evidence on female-specific CVD risk factors is increasing

It's time to act on it and better understand on how to include in our risk estimation.



YOUNGER WOMEN

- Menarche
- PCOS
- OCPs
- Preterm Menopause



PREGNANCY

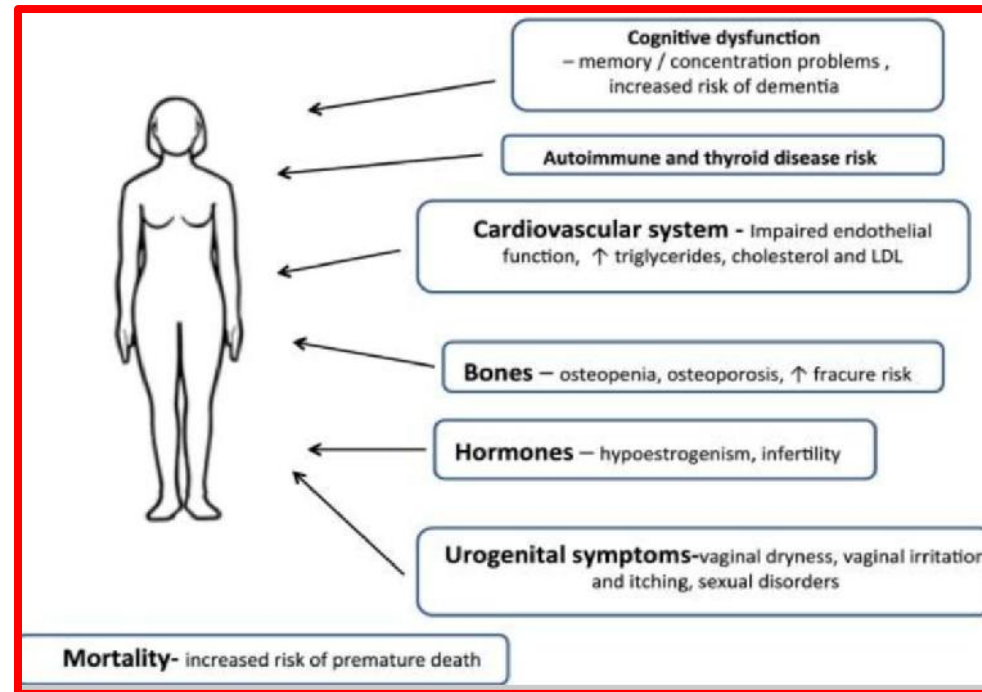
- Gestational diabetes
- Gestational hypertension
- Preeclampsia
- Preterm birth



OLDER WOMEN

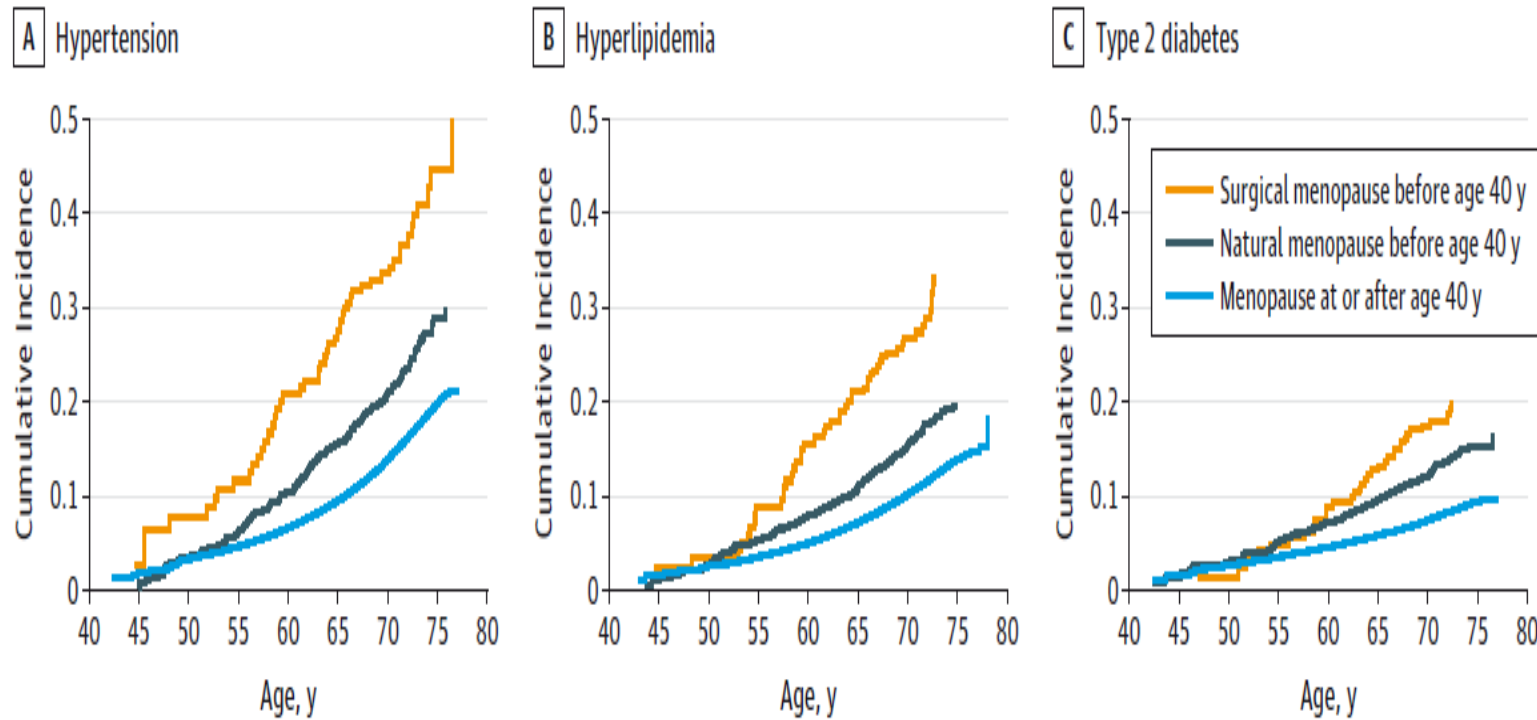
- Menopause
- Hormone replacement therapy

Long term consequences of Premature Ovarian Failure:



The American College of Obstetricians and Gynecologists: Committee on Gynecologic Practice.
Hormone Therapy in Primary Ovarian Insufficiency. Number 698, May 2017

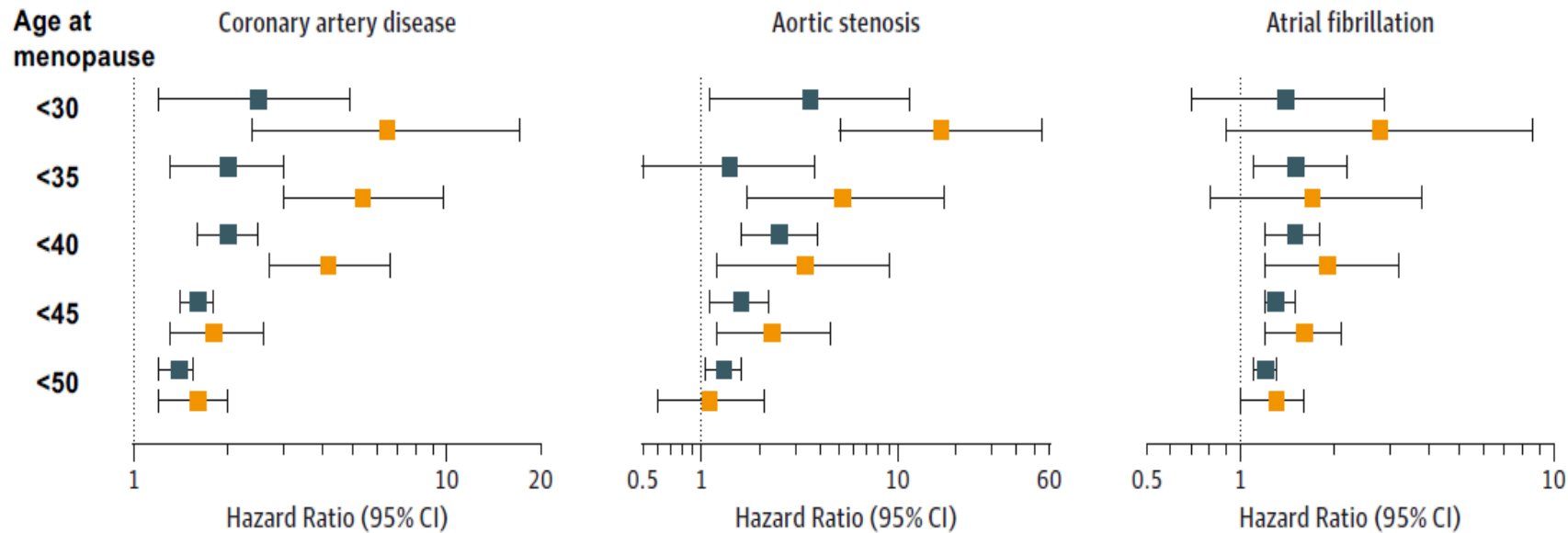
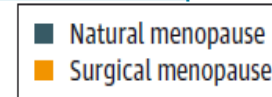
Premature Menopause Leads to Development of CVD Risk Factors



Honigberg MC, et al JAMA 2019)

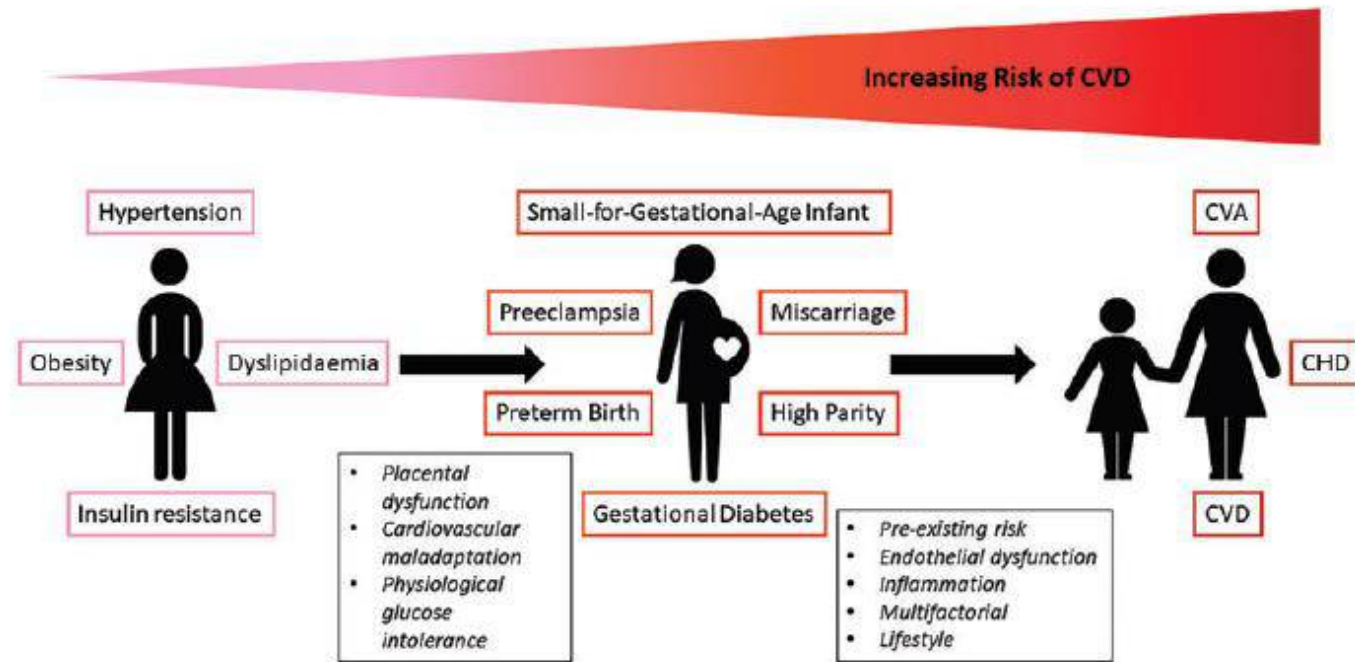
Risk Regardless of Natural or Surgical Menopause

Natural menopause <40 years of age		Surgical menopause <40 years of age	
HR (95% CI)	P-value	HR (95% CI)	P-value
1.36 (1.19-1.56)	<0.001	1.87 (1.36-2.58)	<0.001



Honiabera MC et al.. *JAMA*. 2019.

Potential mechanisms for the association between adverse pregnancy outcomes and future cardiovascular disease risk.



Wu, Mamas, Gulati Women Cardiovasc Health 2019

Adverse pregnancy outcomes and future cardiovascular disease risk

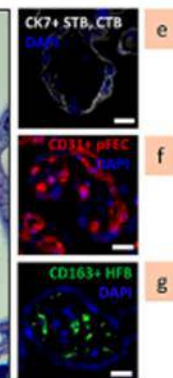
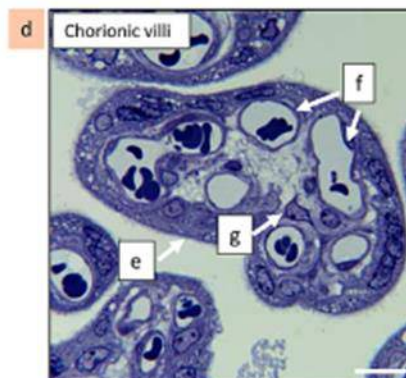
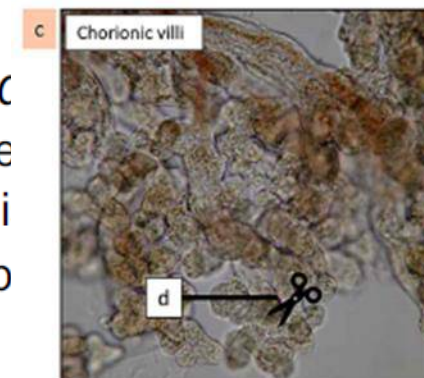
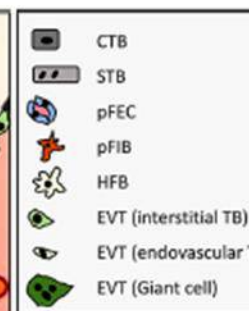
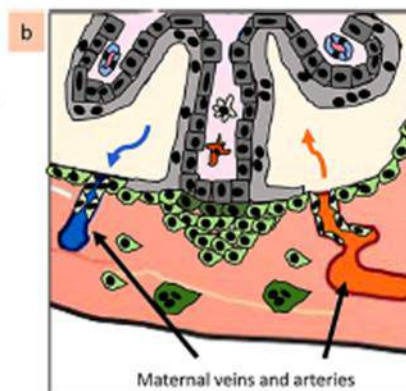
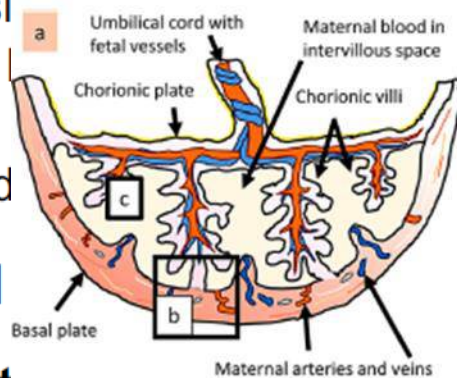
Hypertensive disorders of pregnancy (HDP)

- Preeclampsia
- Gestational hypertension
- Eclampsia
- HELLP syndrome

Gestational hypertension

Preterm birth

- Unclear if increased risk
- Low birth weight
- Stillbirth / miscarriage
- Placental abruption

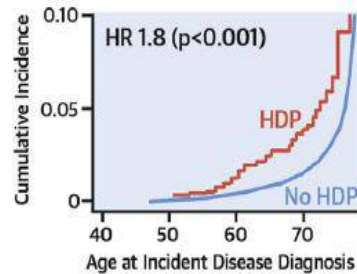
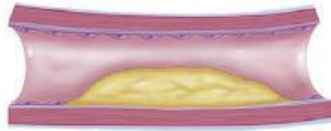


in adverse
vascular events
primary disease and

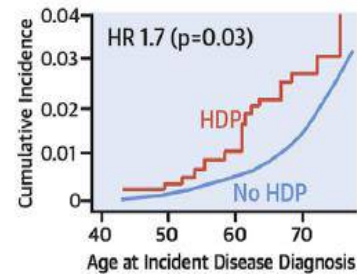
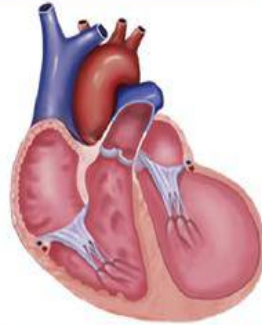
lar risk

CENTRAL ILLUSTRATION Hypertensive Disorders of Pregnancy Are Associated With Long-Term Risk of Diverse Cardiovascular Diseases

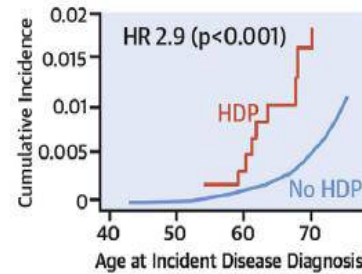
Coronary Artery Disease



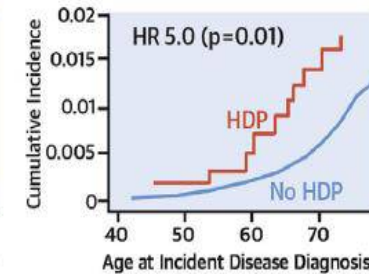
Heart Failure



Aortic Stenosis



Mitral Regurgitation

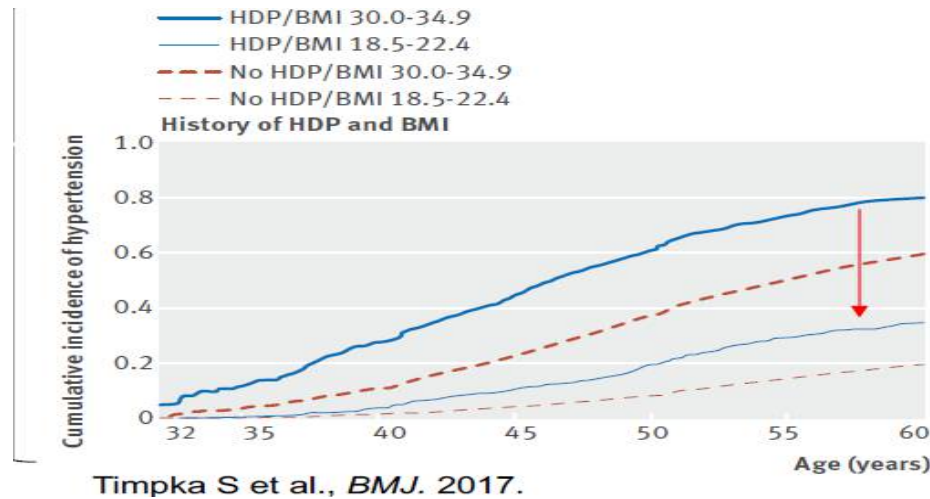


Honigberg, M.C. et al. J Am Coll Cardiol. 2019;74(22):2743-54.

Hypertensive pregnancy was associated with long-term risk of incident coronary artery disease, heart failure, aortic stenosis, and mitral regurgitation. The cumulative incidence plots on the **bottom** reflect incident cardiovascular disease diagnoses among women without each prevalent condition plotted against participant age on the x-axis. The hazard ratios displayed reflect results of the primary survival (Cox proportional hazards) analysis, which were adjusted for age at study enrollment and race.

Development of Chronic HTN Mediates CVD Risk in Women with HDP

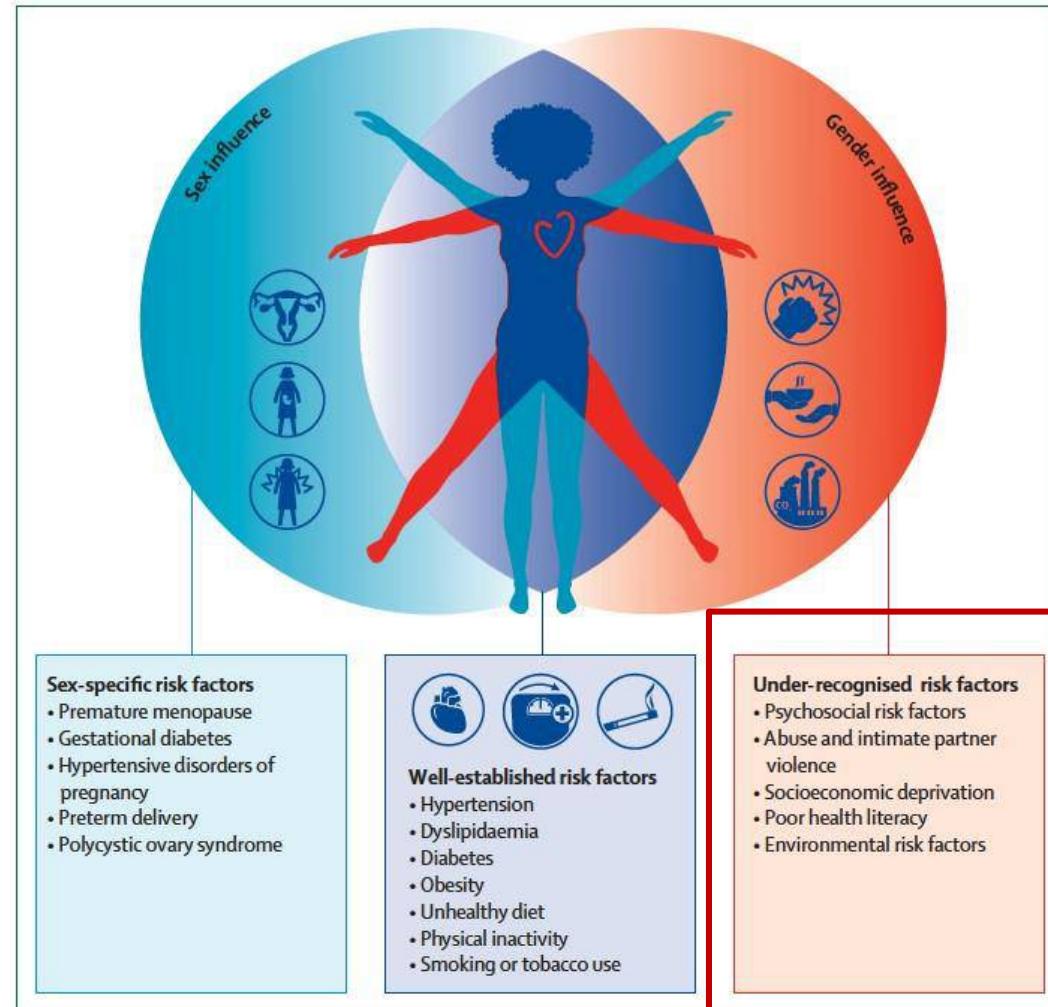
- Chronic HTN responsible for 50-80% of excess CVD risk
- Maintenance of normal weight may prevent or delay onset of chronic HTN after HDP



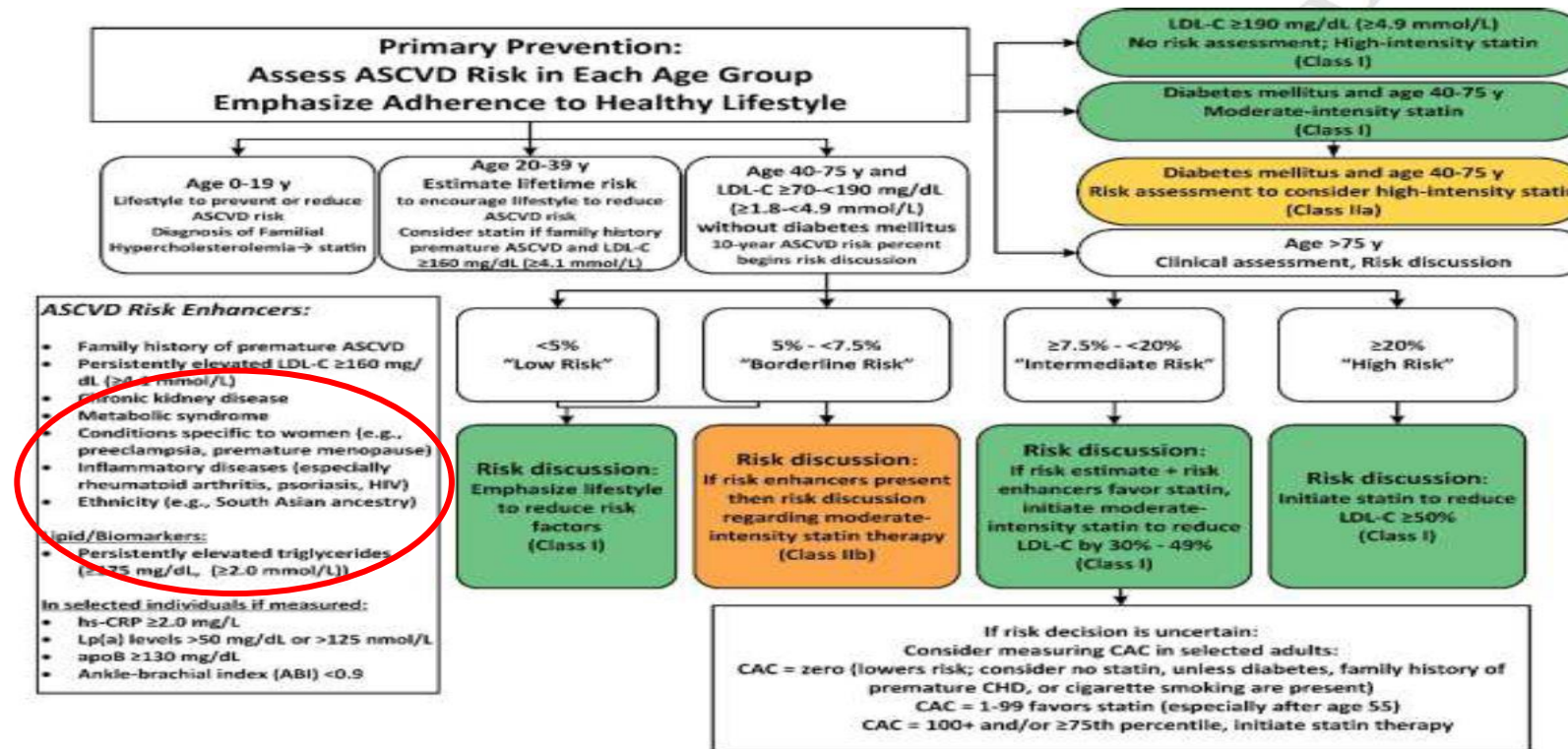
Honigberg MC et al., *J Am Coll Cardiol*. 2019.
Haug EB et al., *JAMA Cardiol*. 2019.

7. Many CVD risk factors in women are still under-recognized

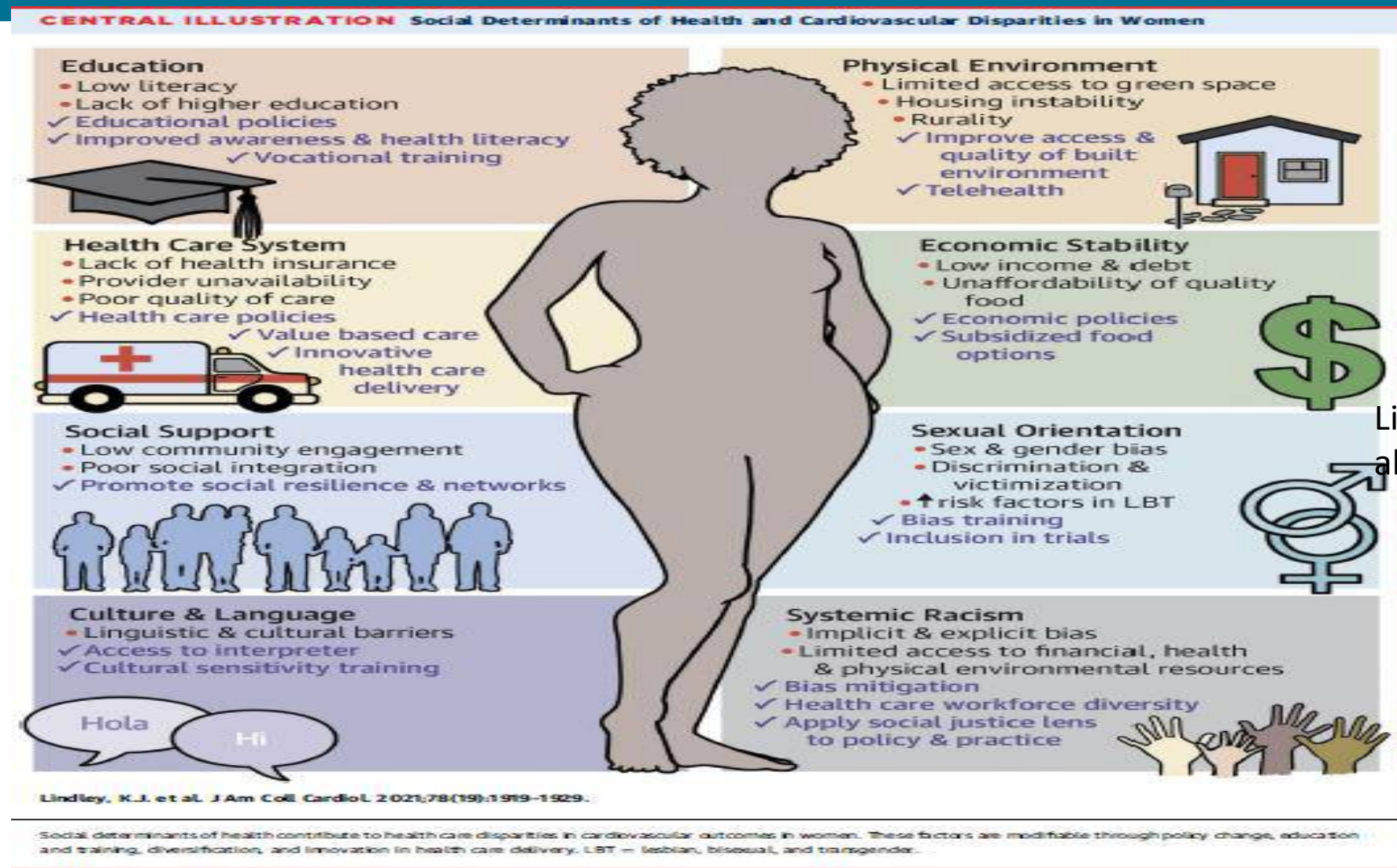
...and strongly associated with female gender and the interaction with a woman's social and physical environment



2018 Lipid Guidelines: Risk Assessment – Primary Prevention



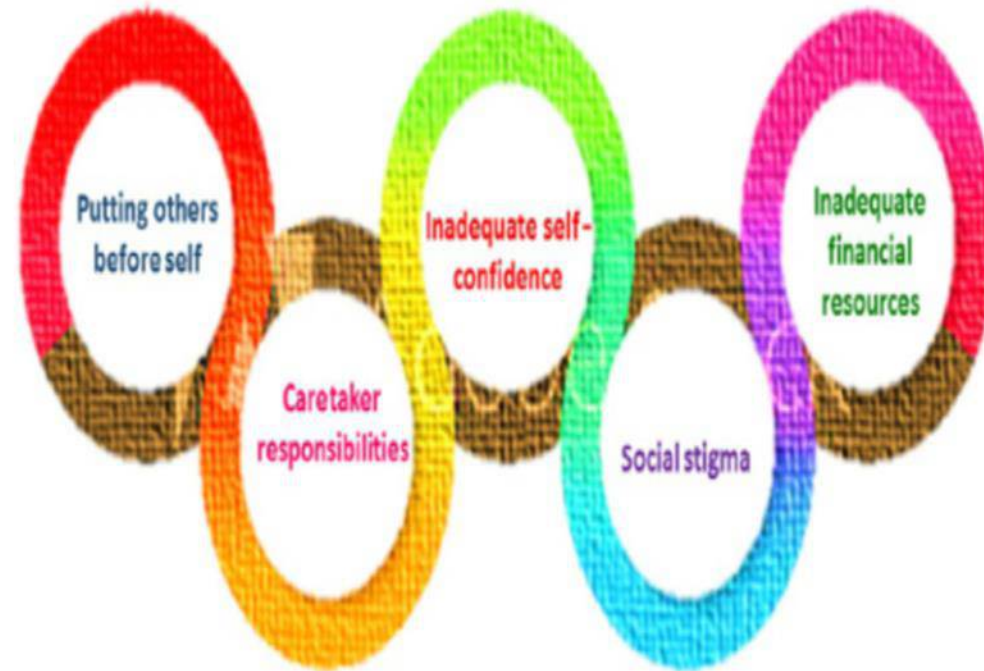
8. Social Determinants of Health of Critical Importance



Socioeconomic

Unhealthy

 Congenital heart disease



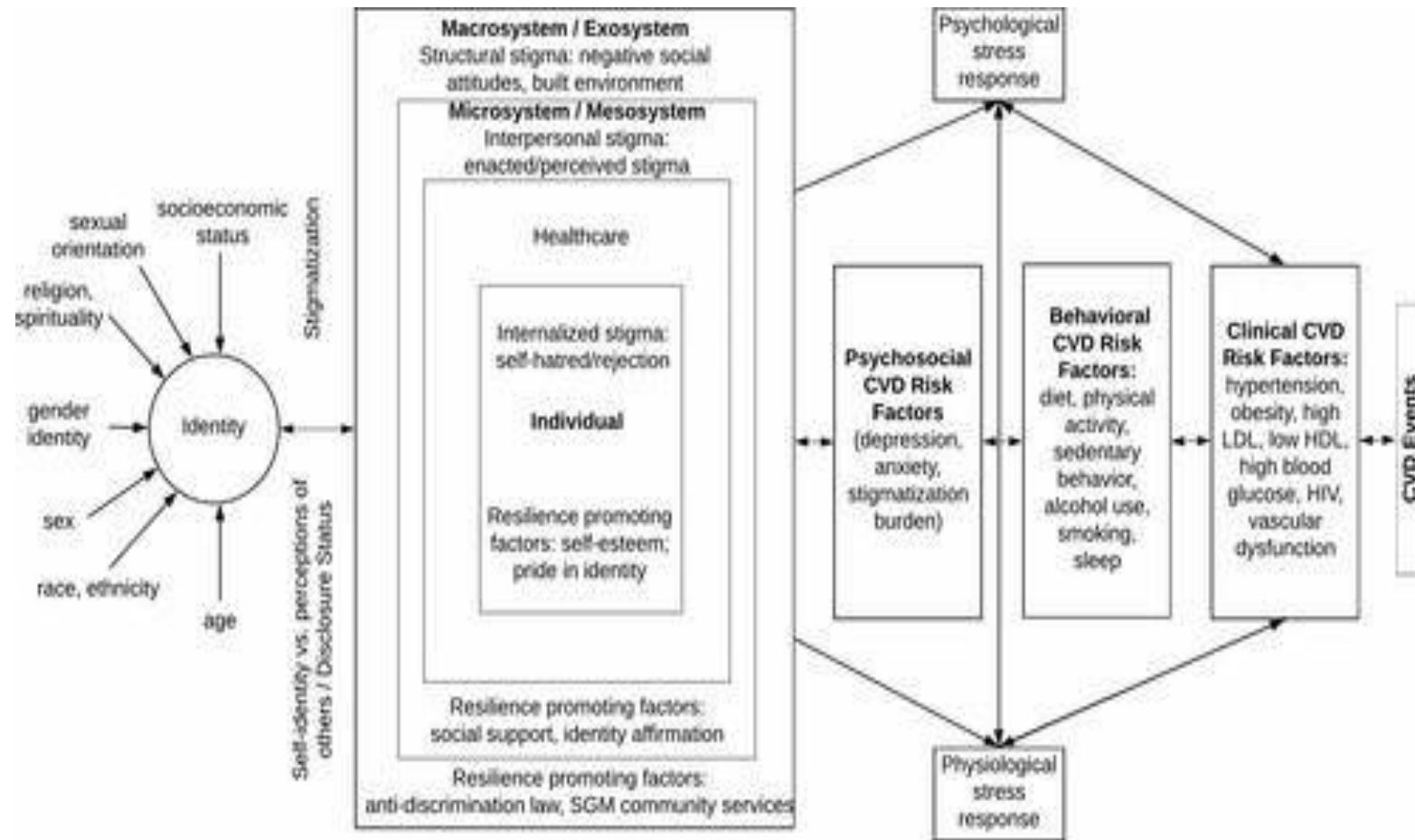
Depression and social isolation



- Coronary artery disease
- Heart failure
- Dementia
- Metabolic syndrome
- Atrial fibrillation
- Stroke
- Cancer treatment associated heart disease
- HFpEF > HFrEF

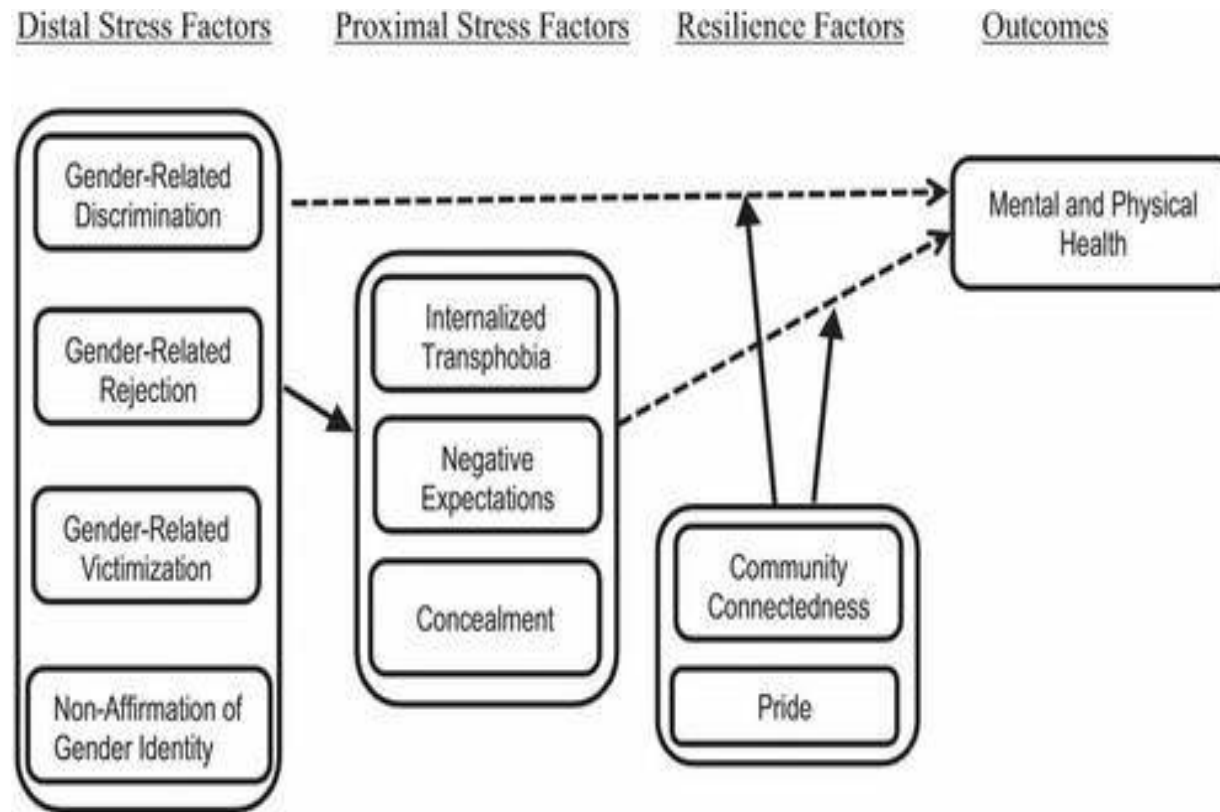
FIGURE 4 Potential Barriers for Women Seeking Care. Women often do not prioritize their cardiovascular health and reported several barriers that account for this behavioral trend. *Data from [11].*

Transgender CV Health



Carl G. Streed. *Circulation*. Assessing and Addressing Cardiovascular Health in People Who Are Transgender and Gender Diverse: A Scientific Statement From the American Heart Association, Volume: 144, Issue: 6, Pages: e136-e148, DOI: (10.1161/CIR.0000000000001003)

Gender Minority Stress and Resilience Model



Carl G. Streed. *Circulation*. Assessing and Addressing Cardiovascular Health in People Who Are Transgender and Gender Diverse: A Scientific Statement From the American Heart Association, Volume: 144, Issue: 6, Pages: e136-e148, DOI: (10.1161/CIR.0000000000001003)