

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

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Cardiology

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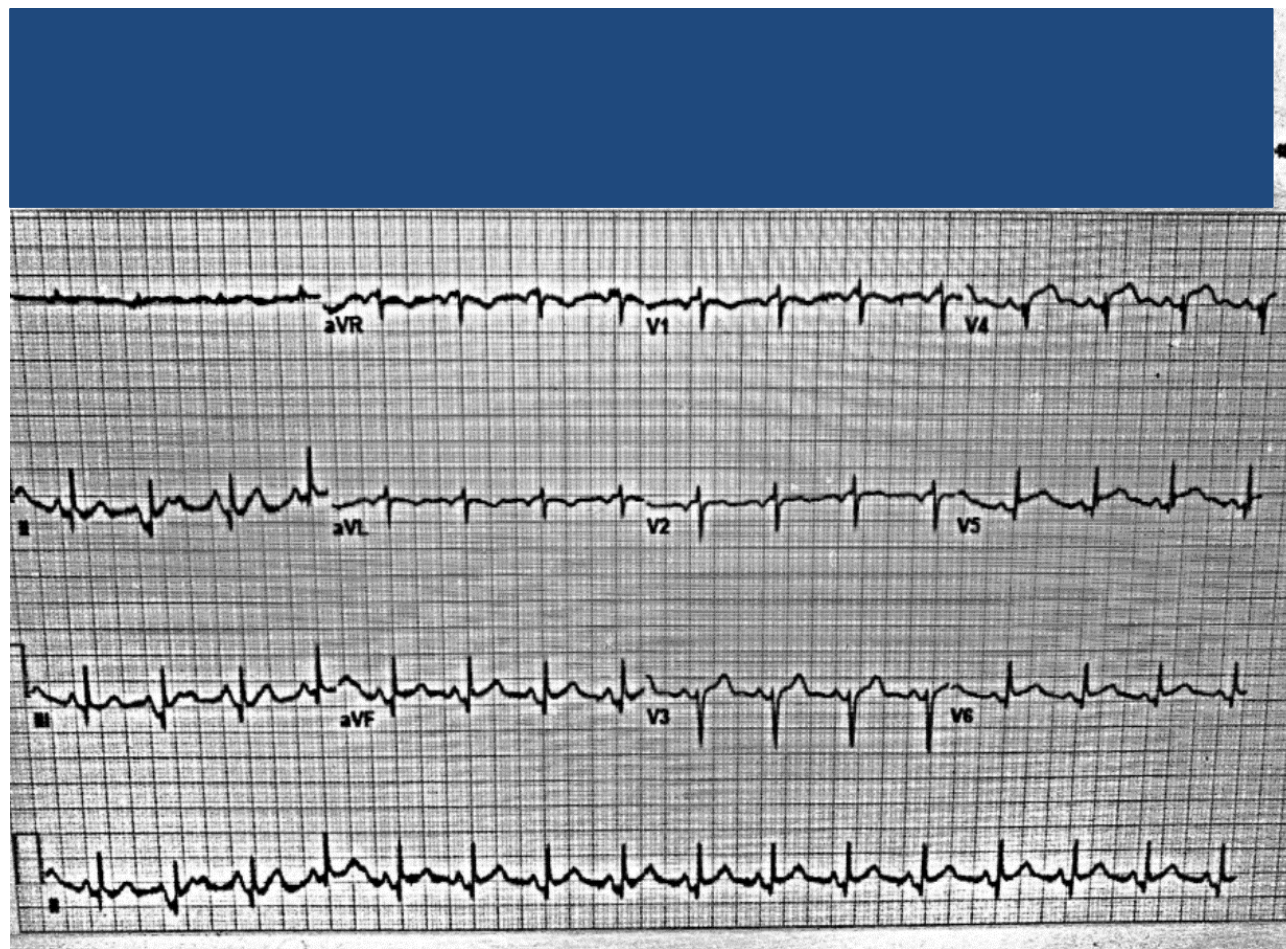
@drmalissawood

# **Two Cases, Two ECG's, Two Lessons**

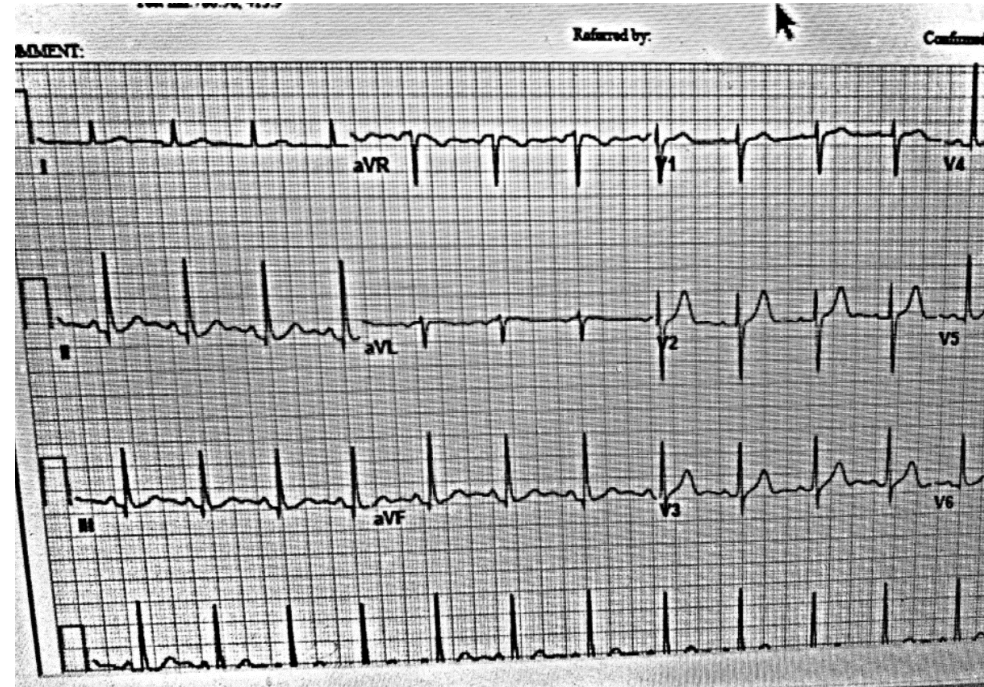
# A 58 yo F presents with chest pain...

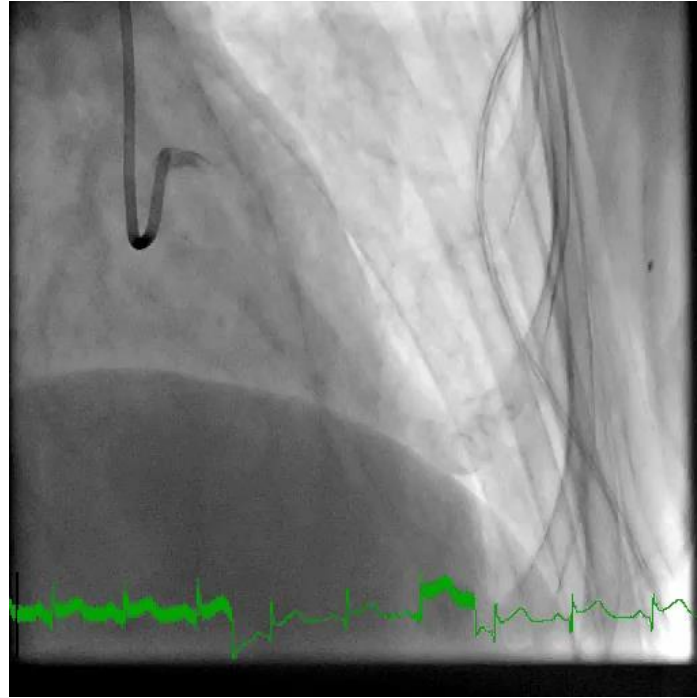
- PMH:
  - Preeclampsia x 2
  - Anxiety
  - Prior Takotsubo episodes in setting of emotional stress 1998, 2007 (cath both times @ OSH)
- Referred to Corrigan Women's Heart Health program by her outside cardiologist for "routine" evaluation, review of data but did not make appt since she was feeling fine
- Went to BHI and completed course several years ago but does follow the recommended plans, declined SSRI
- Most recent cardiac testing: 2018 TTE with normal LVEF, ETT 11 METS no ischemia
  - 5/20 Recent stressors, much worsened on day of admission
  - Chest pressure, SOB → ECG obtained in the ED
  - hsTNT 2297

# Current ECG



# Prior ECG



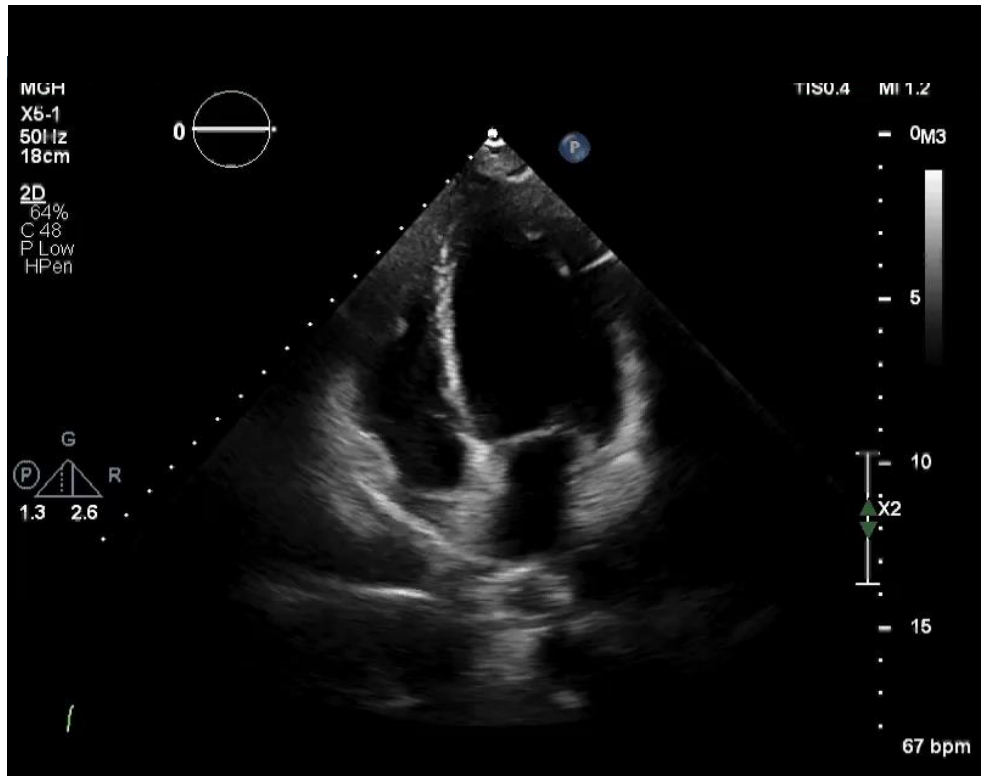




# **Lesson**

- **Always look for old ECG's when evaluating a patient with chest discomfort or abnormal ECG**





# History of Present Illness

- CC: Postoperative dyspnea and hypoxia

- History of Present Illness:

- 35-year-old woman, G2P2 in 30<sup>th</sup> week of pregnancy presented with premature labor
- Complained of chest discomfort while on the OB floor, treated for GERD
- Developed fetal distress → taken to OR for urgent C-section
  - Successful delivery, but...

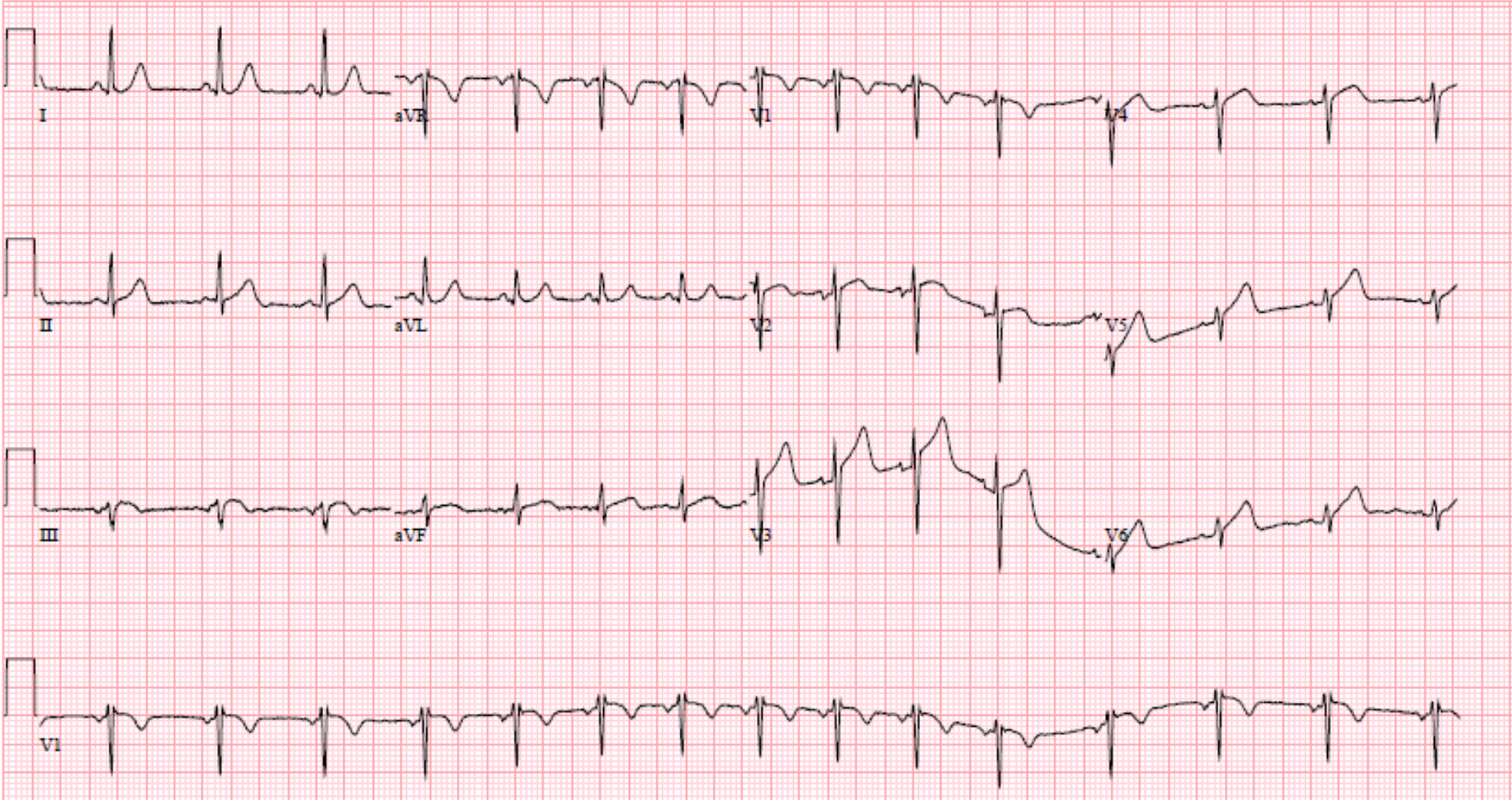
# HPI, continued

“...the patient began coughing upon leaving the Operating Room, and the coughing was more pronounced with coughing paroxysms in the Recovery Room. Her **O2 saturations began to drop into the mid 80s** and at one point down to 78. At this time, she was **tachycardic at 130 to 140** and a physical exam disclosed **rales in both lung fields**. The patient was placed on a nonrebreather oxygen mask and given 20 mg of Lasix IV immediately. She had a very good diuretic response. Her oxygen saturation improved and her lung exam improved as well. ”

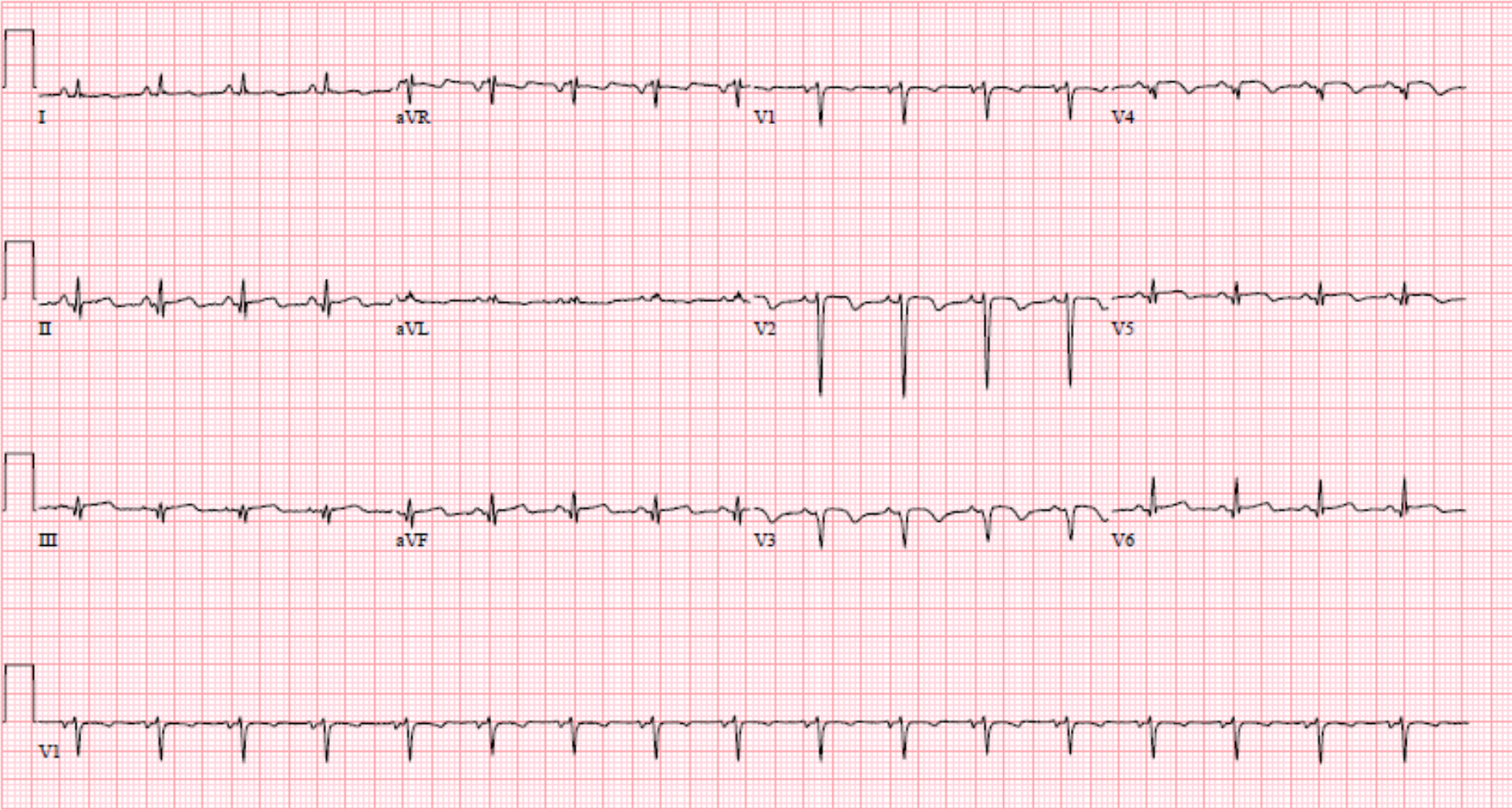
# HPI, continued

- Admitted to obstetrics floor
- Diuresis continued
- Febrile → treated for endometritis
- ECG ordered at 10:05 PM

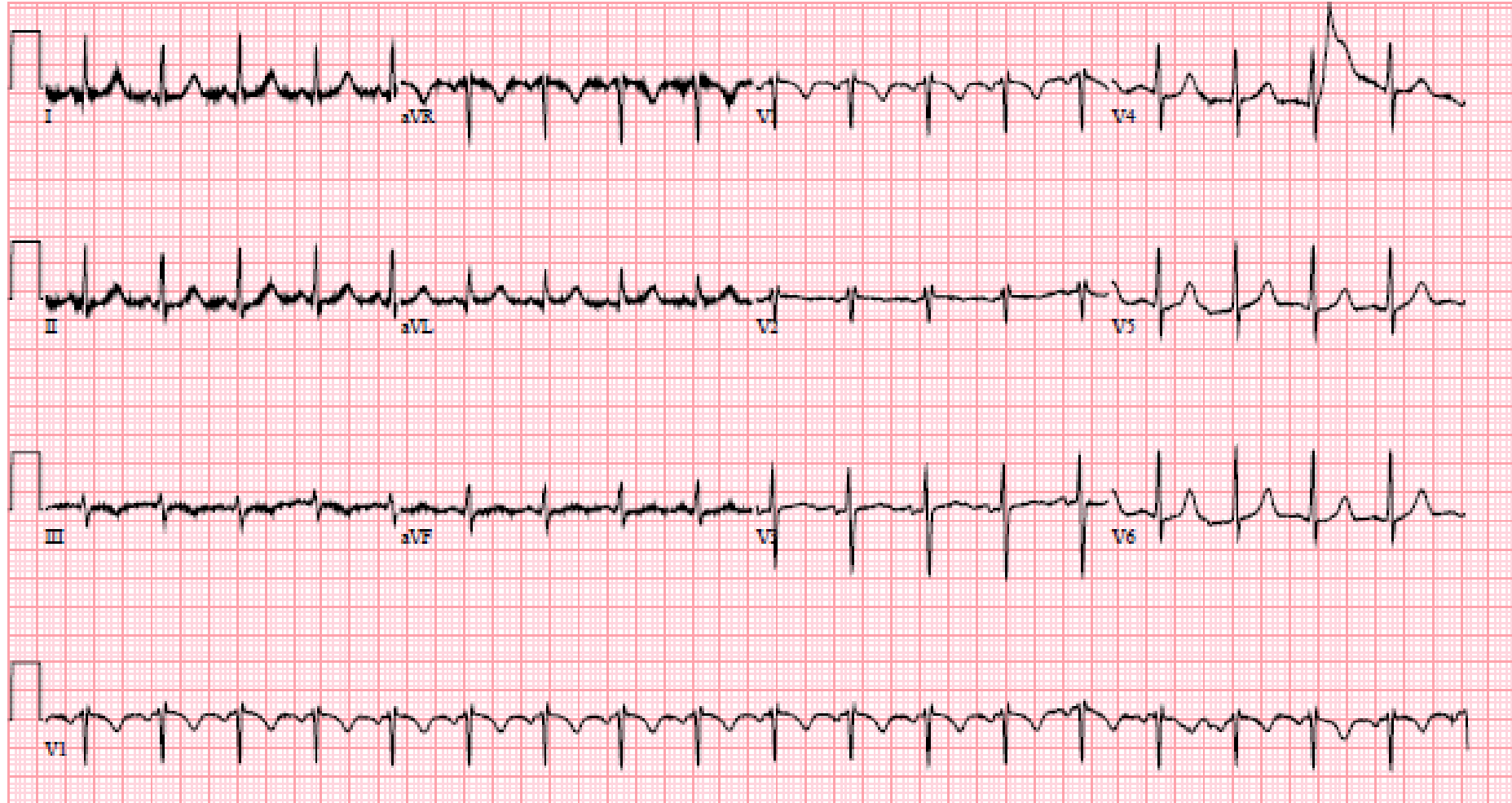
**Intern noticed ECG from prior evening in chart and brought it to ordering resident at 3:00 AM**



# 3:30 AM ECG



# Baseline ECG 2 months PTA

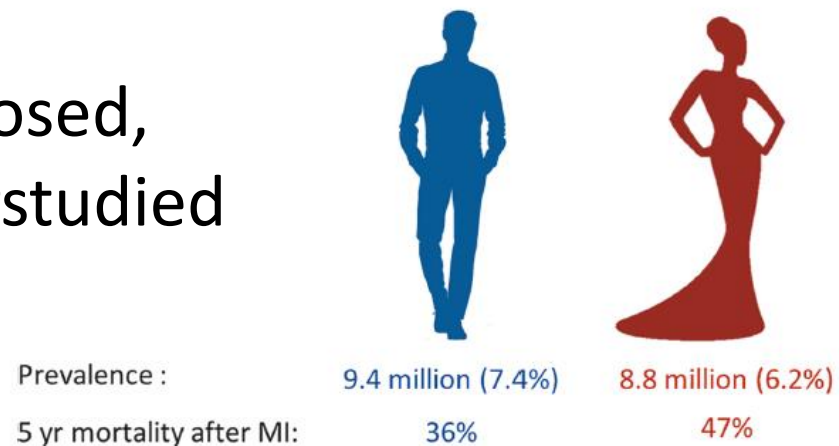


# Lesson

- Follow up on any tests you order
- If you are worried enough to order an ECG in the post-partum unit, make sure you look at it as soon as it is completed!
- Always review prior ECG's when available



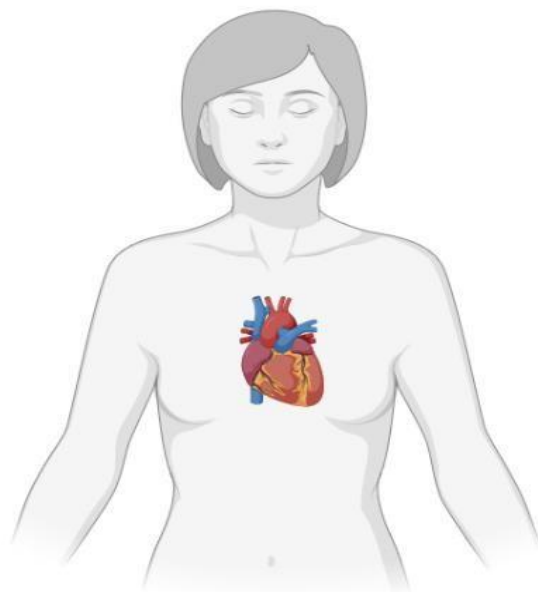
- 9 million women died from CVD in 2019
- CV disease responsible for 35% of deaths in women worldwide
- Stagnation in previously favorable CVD trends
  - Women are underdiagnosed, undertreated and understudied



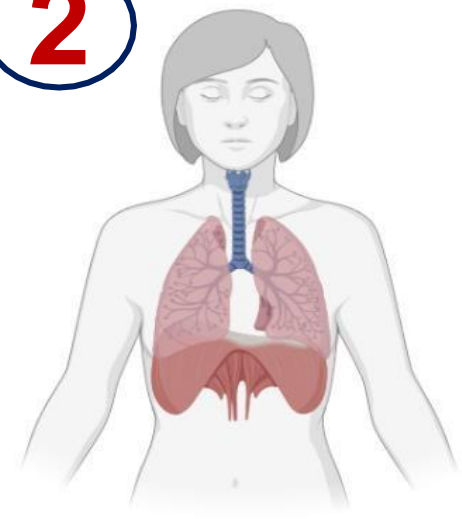
# 1. Cardiovascular disease is the leading cause of mortality in women

1

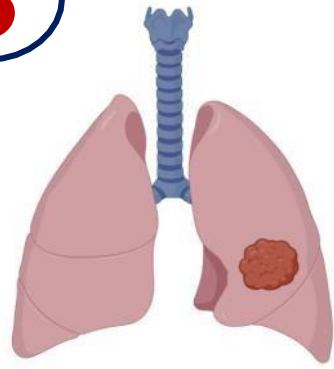
Total Deaths in Women in USA 2016: 1,236,003



2



3



4



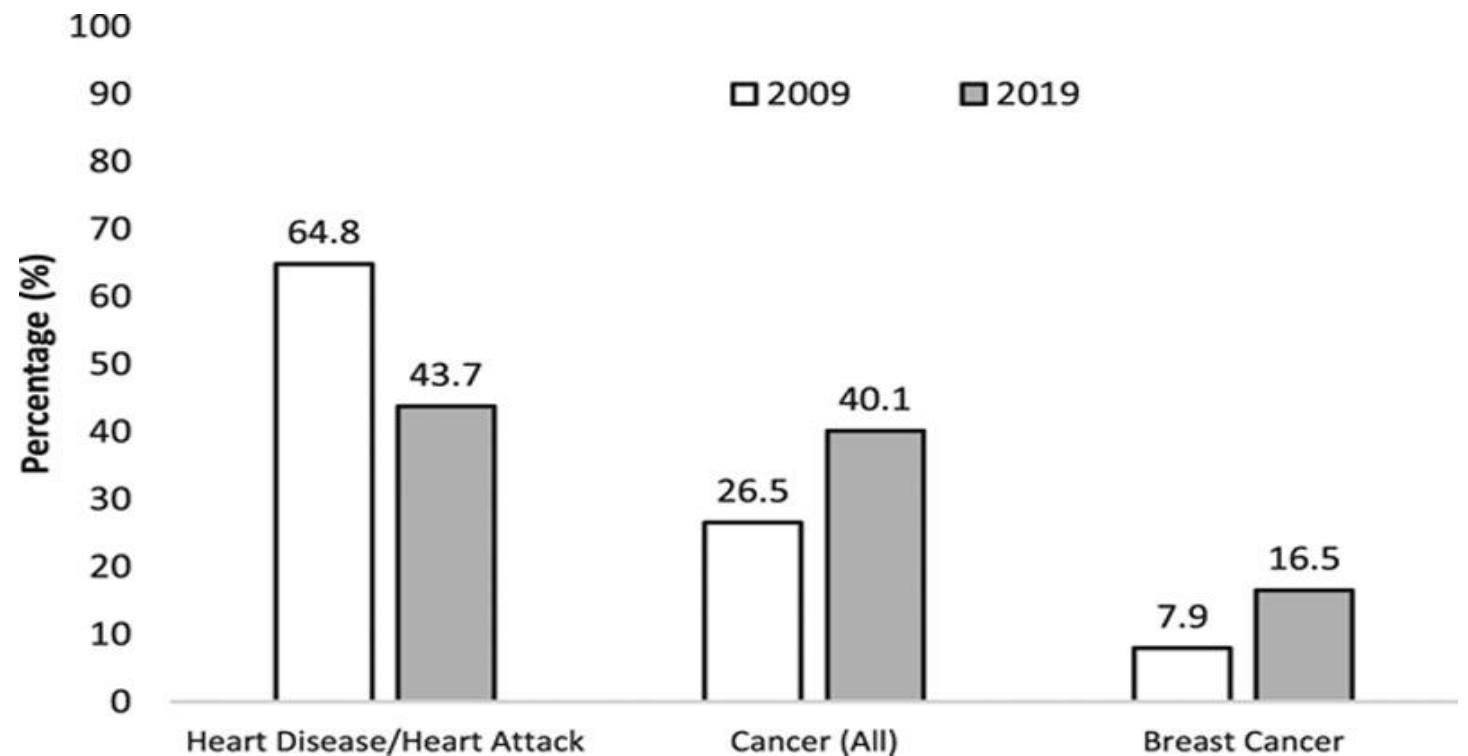
<b>Cardiovascular disease</b> 412,244 deaths	<b>Chronic Lung Disease</b> 81,551 deaths	<b>Lung Cancer</b> 70,500 deaths	<b>Breast Cancer</b> 40,920 deaths
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Slides courtesy of Dr. Roxana Mehran  
Benjamin EJ et al., Circulation 2019

## 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

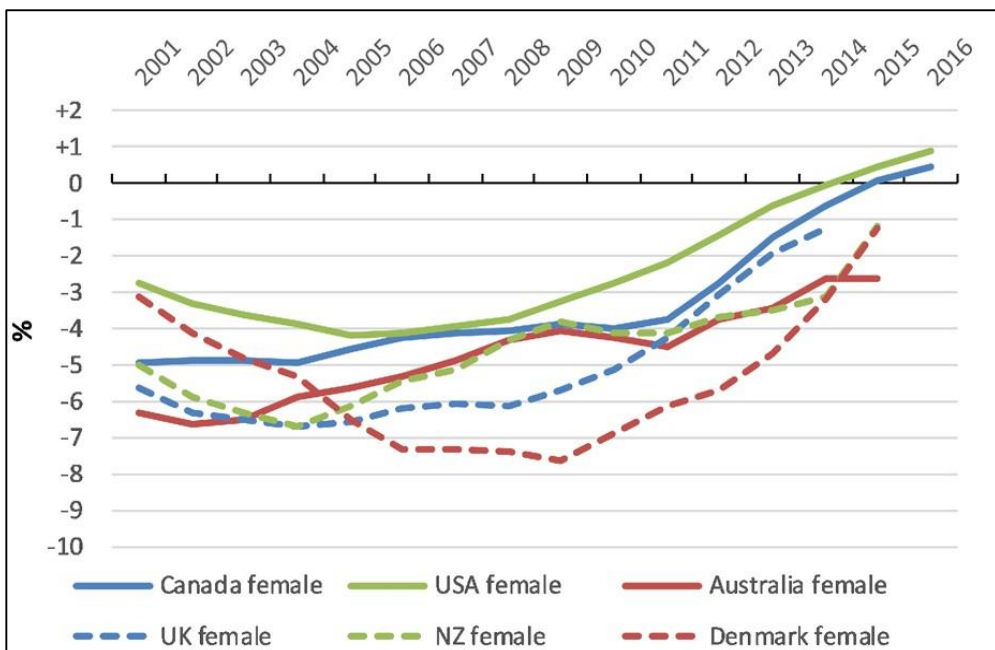
**THE TRIAL**

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

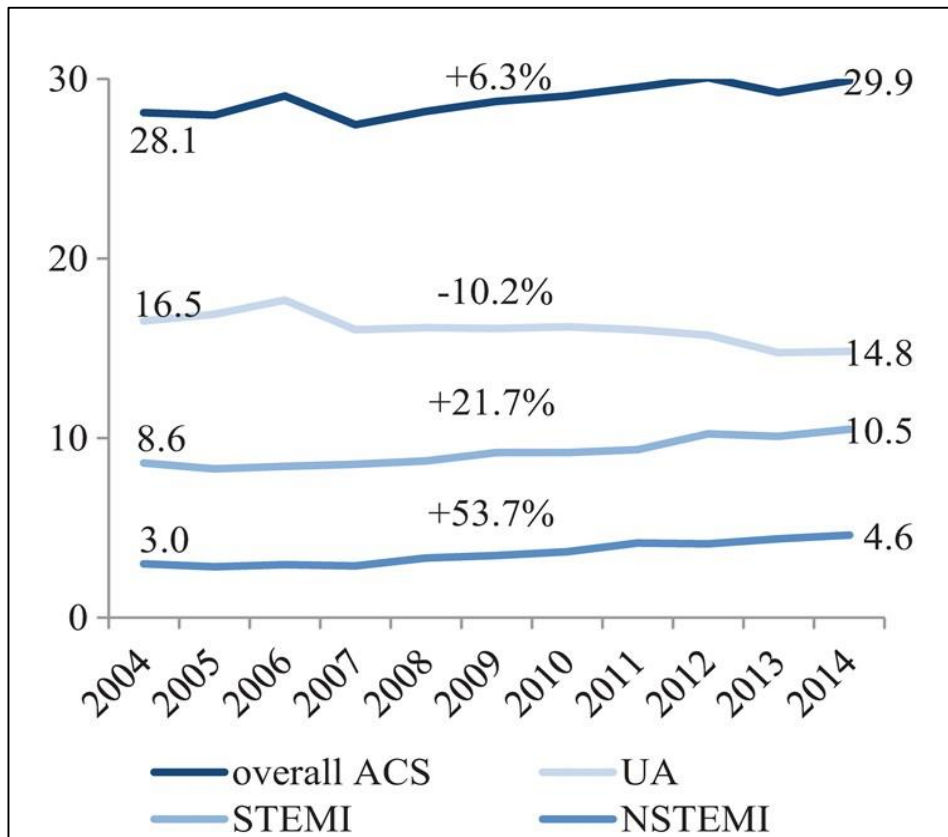
# 4. In high-income regions, the decline in CVD mortality has slowed and CVD mortality has increased in women from certain countries



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.

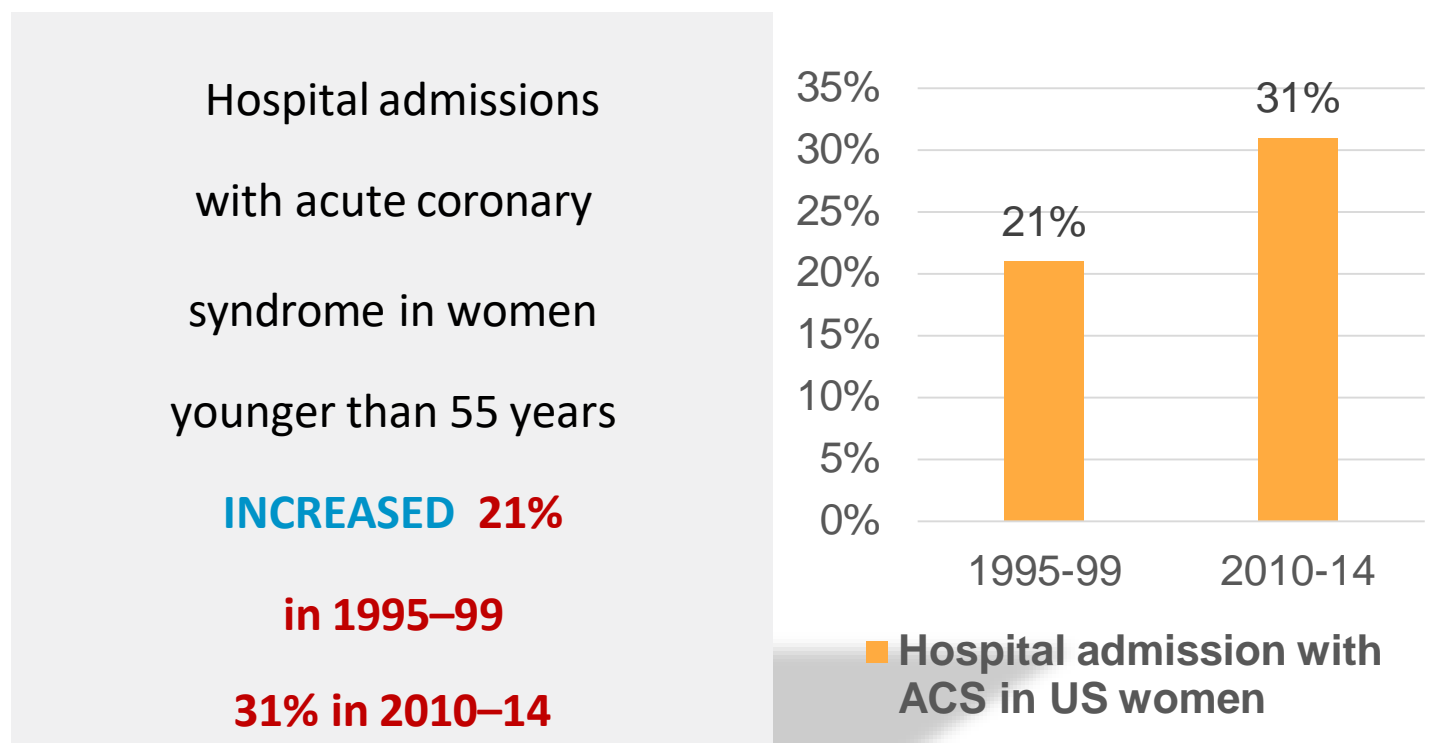
# 5. There is an increase in myocardial infarction in young women

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  $\leq 50$

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


# 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



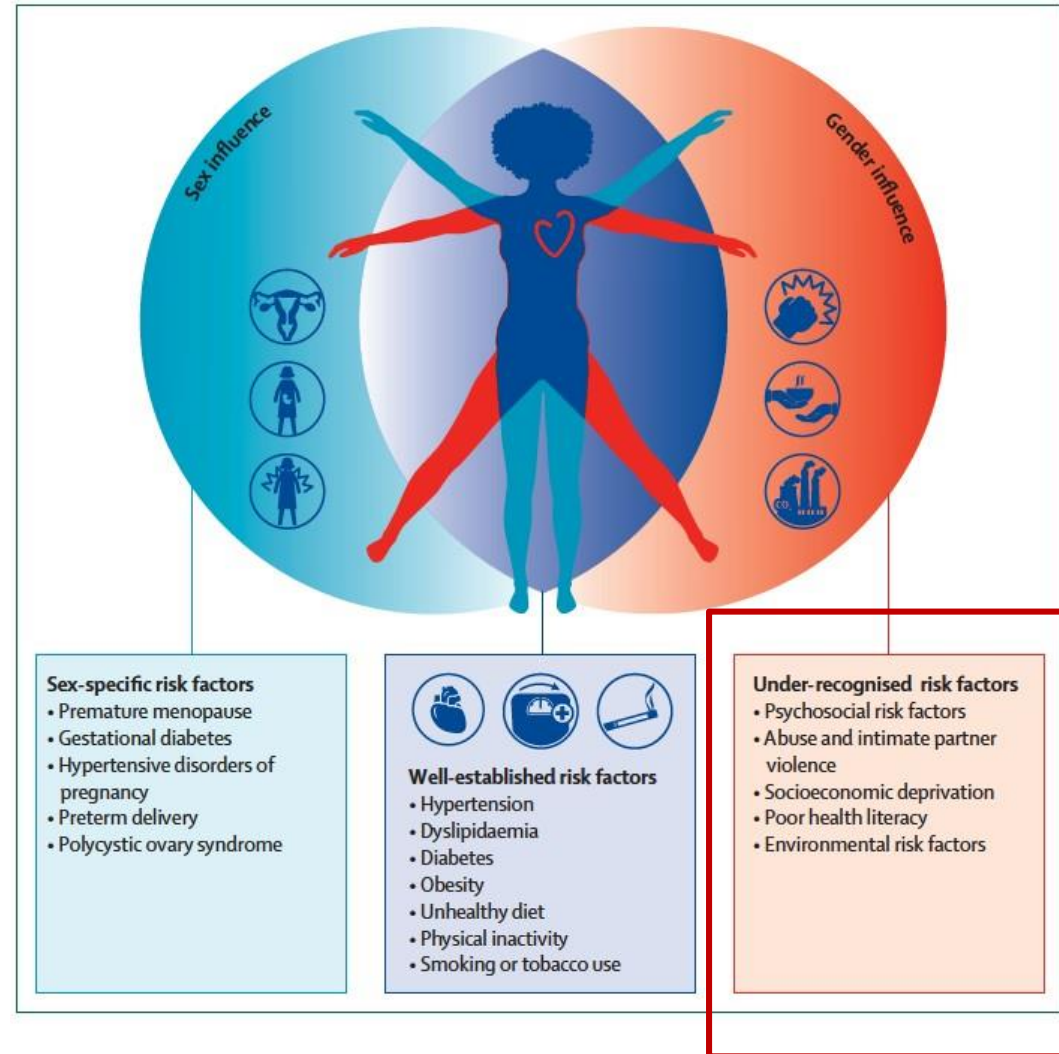
**OLDER WOMEN**

- Menopause
- Hormone replacement therapy

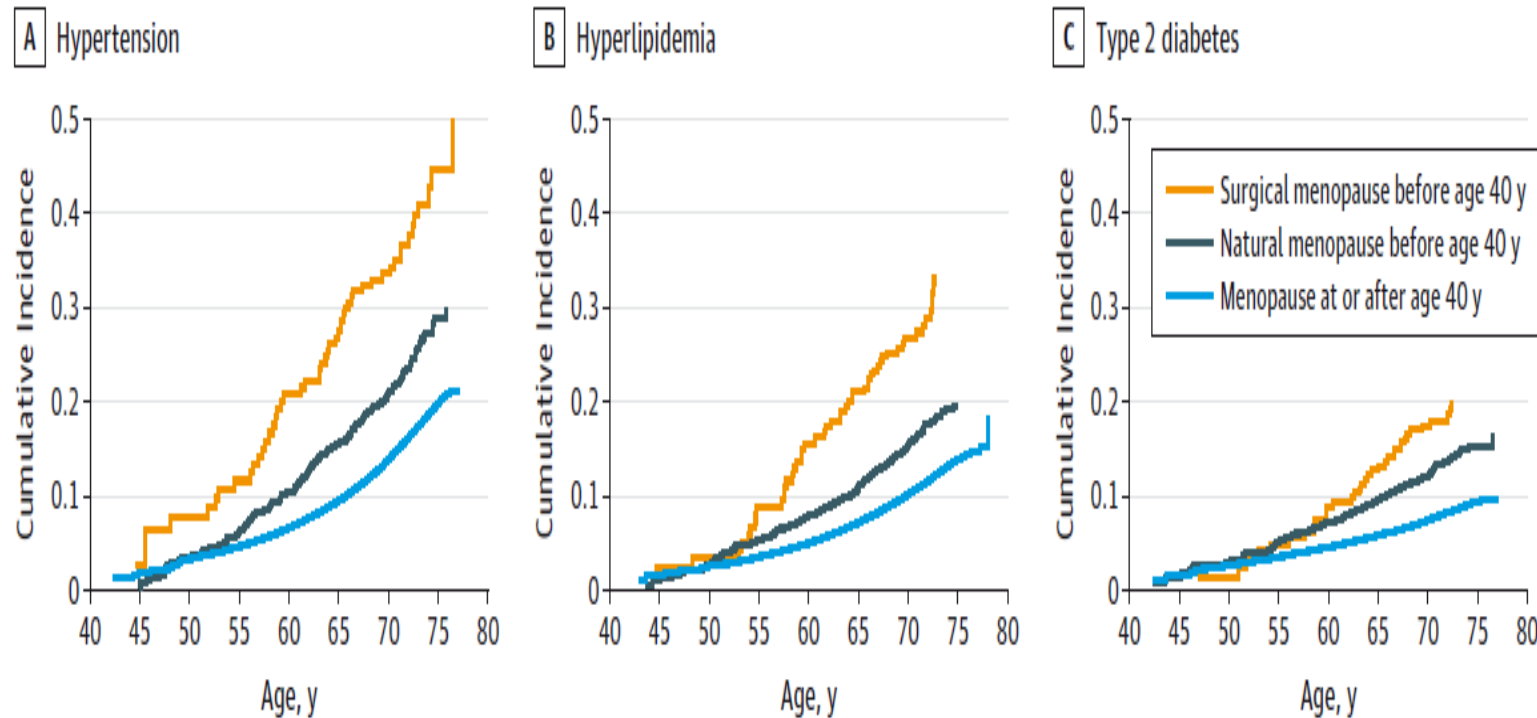


# 7. Many CVD risk factors in women are still under-recognized

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



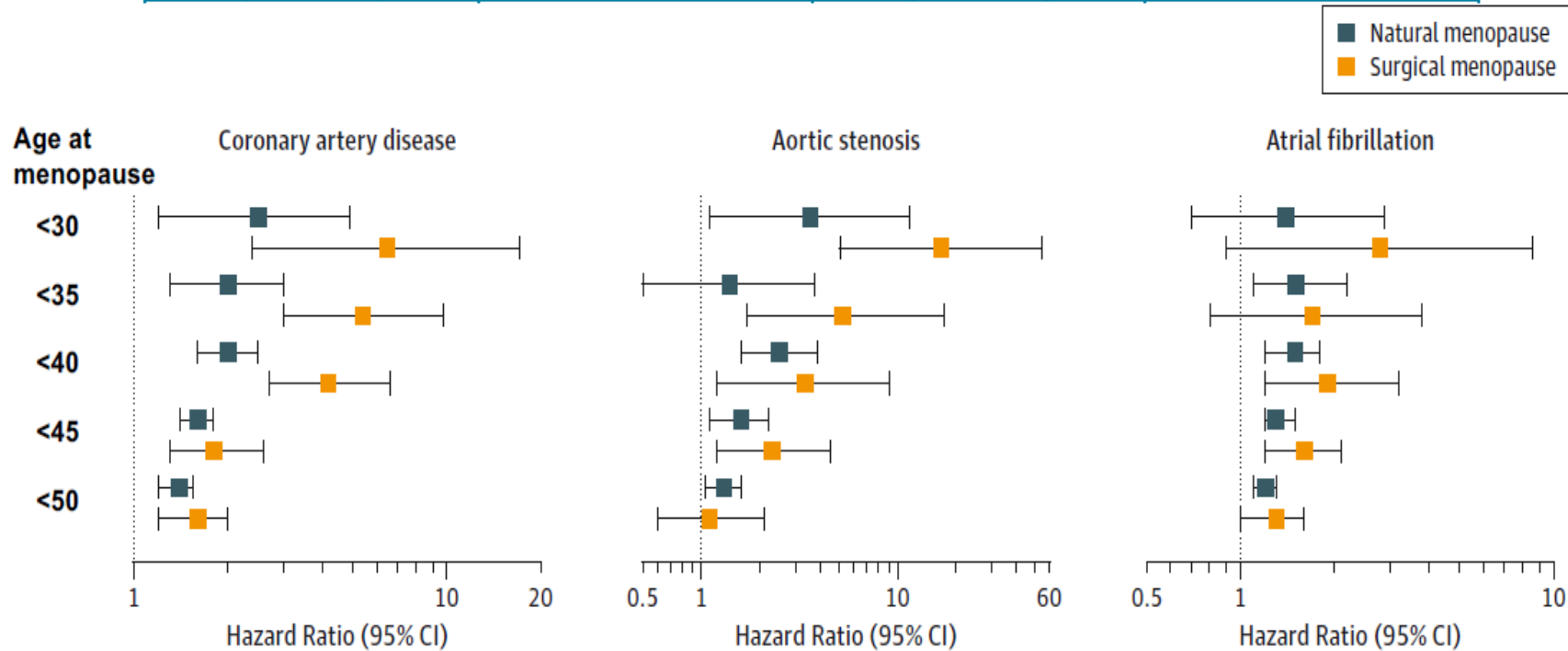
# Premature Menopause Leads to Development of CVD Risk Factors



Honigberg MC, et al JAMA 2019)

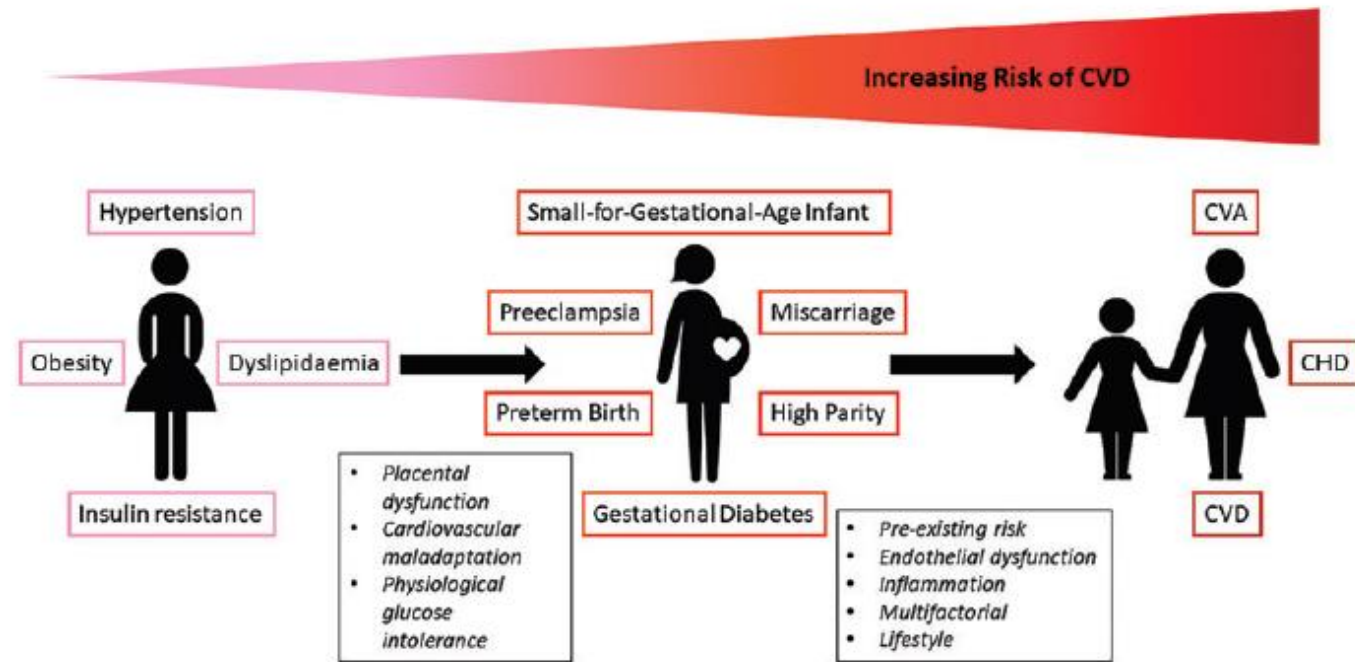
# Risk Regardless of Natural or Surgical Menopause

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

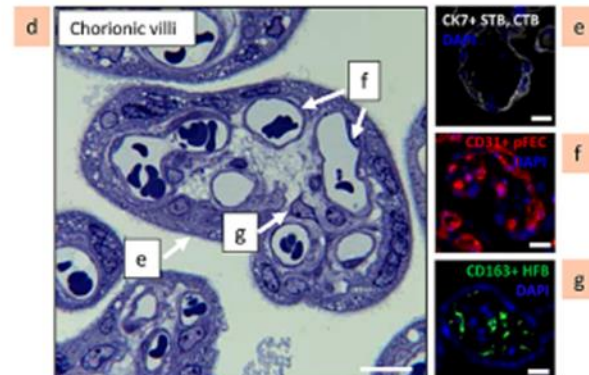
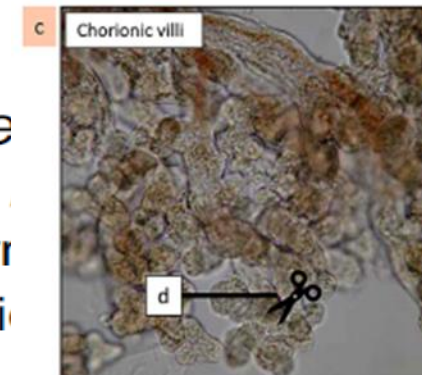
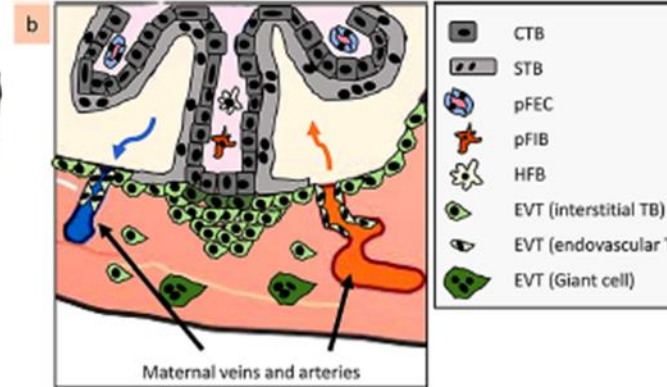
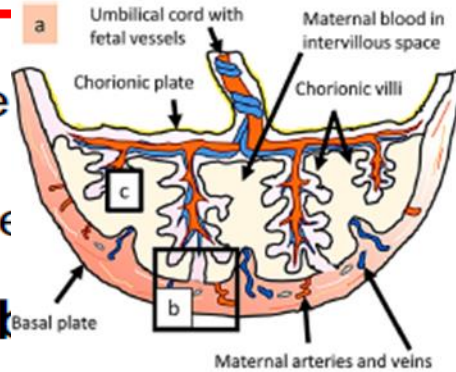
## Hypertensive disorders of pregnancy (HDP)

- Preeclampsia
- Gestational hypertension
- Eclampsia
- HELLP syndrome

## Gestational diabetes

## Preterm birth

- Unclear if independent
- Low birth weight
- Stillbirth / miscarriage
- Placental abruption



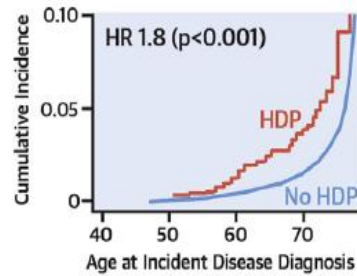
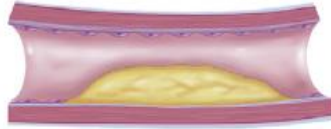
1.5-2x ↑ in adverse cardiovascular events (coronary disease and stroke)

cardiovascular risk

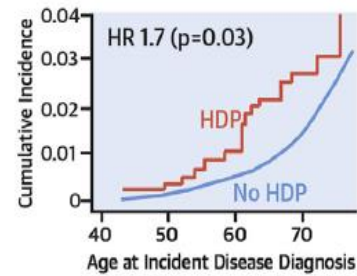
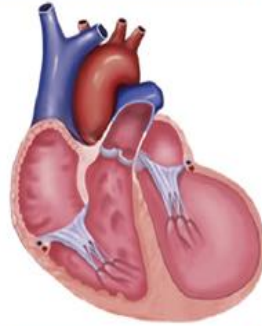


**CENTRAL ILLUSTRATION** Hypertensive Disorders of Pregnancy Are Associated With Long-Term Risk of Diverse Cardiovascular Diseases

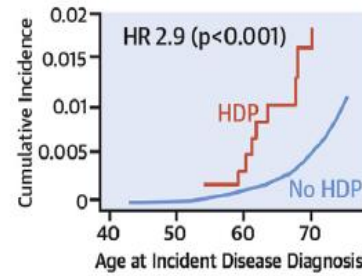
**Coronary Artery Disease**



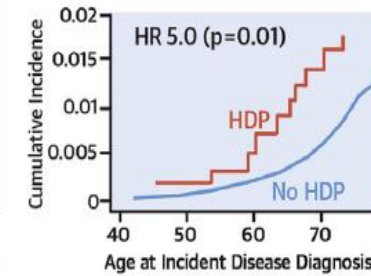
**Heart Failure**



**Aortic Stenosis**



**Mitral Regurgitation**

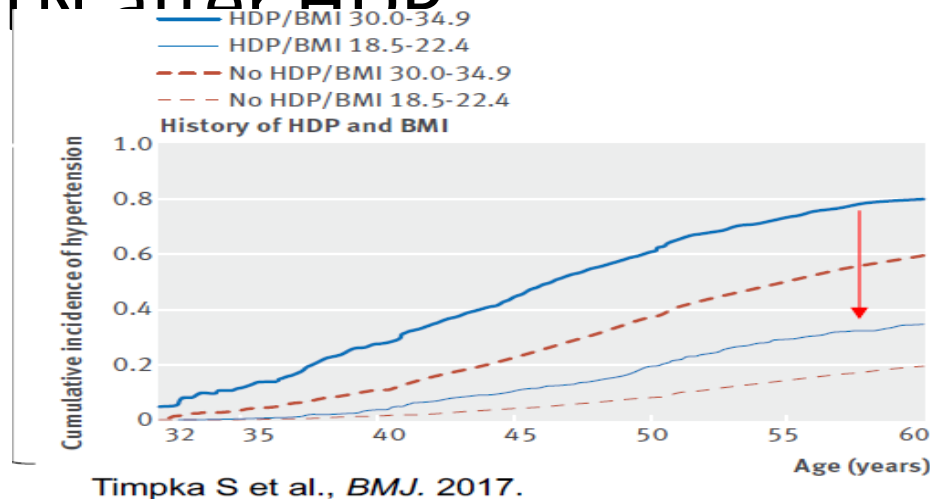


Honigberg, M.C. et al. J Am Coll Cardiol. 2019;74(22):2743-54.

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.

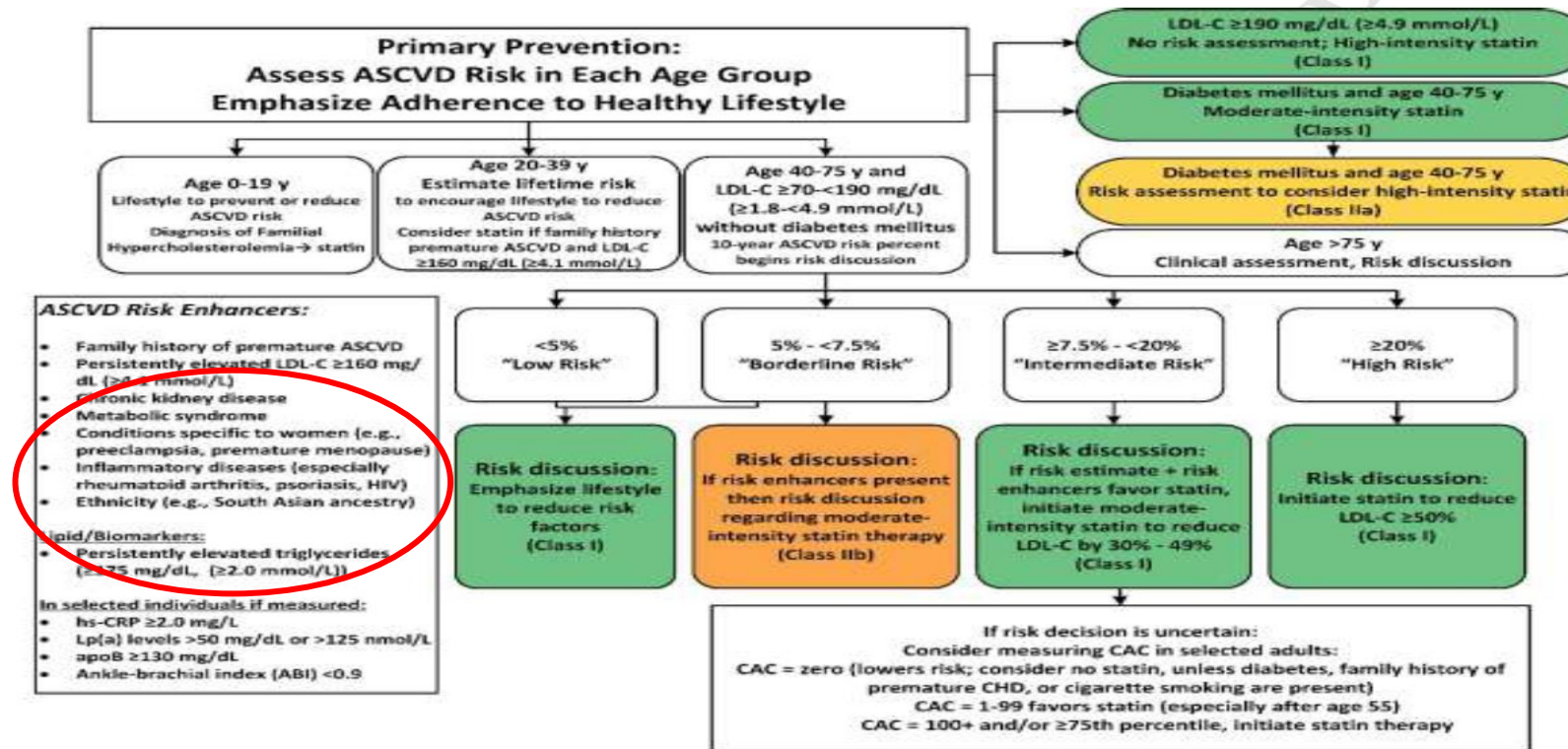
# Development of Chronic HTN Mediates CVD Risk in Women with HDP

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



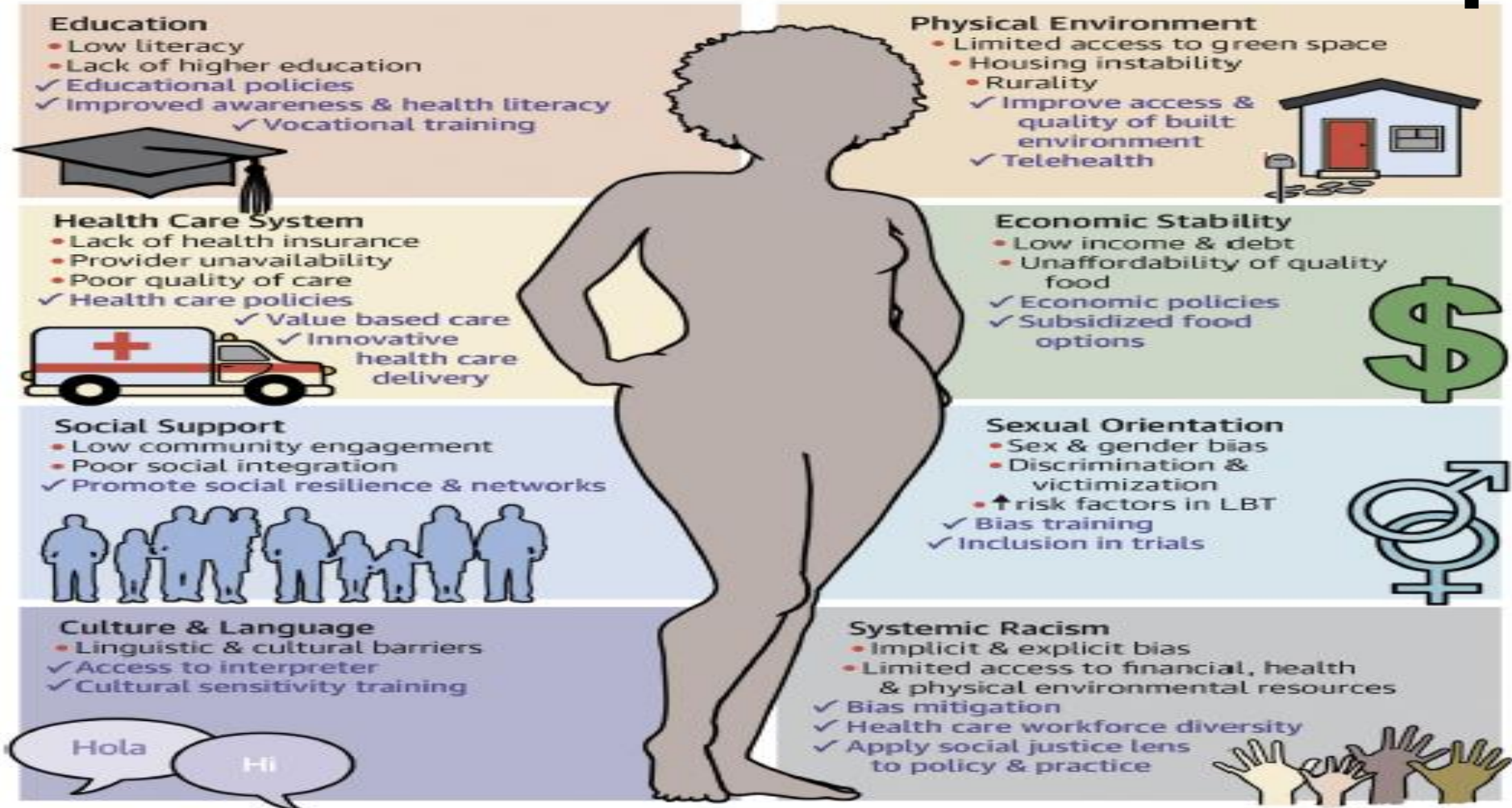
Honigberg MC et al., *J Am Coll Cardiol*. 2019.  
Haug EB et al., *JAMA Cardiol*. 2019.

# 2018 Lipid Guidelines: Risk Assessment – Primary Prevention





# 8. Social Determinants of Health of Critical Importance



Lindley, K.J. et al. J Am Coll Cardiol. 2021;78(19):1919-1929.

Social determinants of health contribute to health care disparities in cardiovascular outcomes in women. These factors are modifiable through policy change, education and training, diversification, and innovation in health care delivery. LBT = lesbian, bisexual, and transgender.

Lindley,  
Wood et al  
JACC 2021

# So many opportunities to deliver comprehensive care and intervene

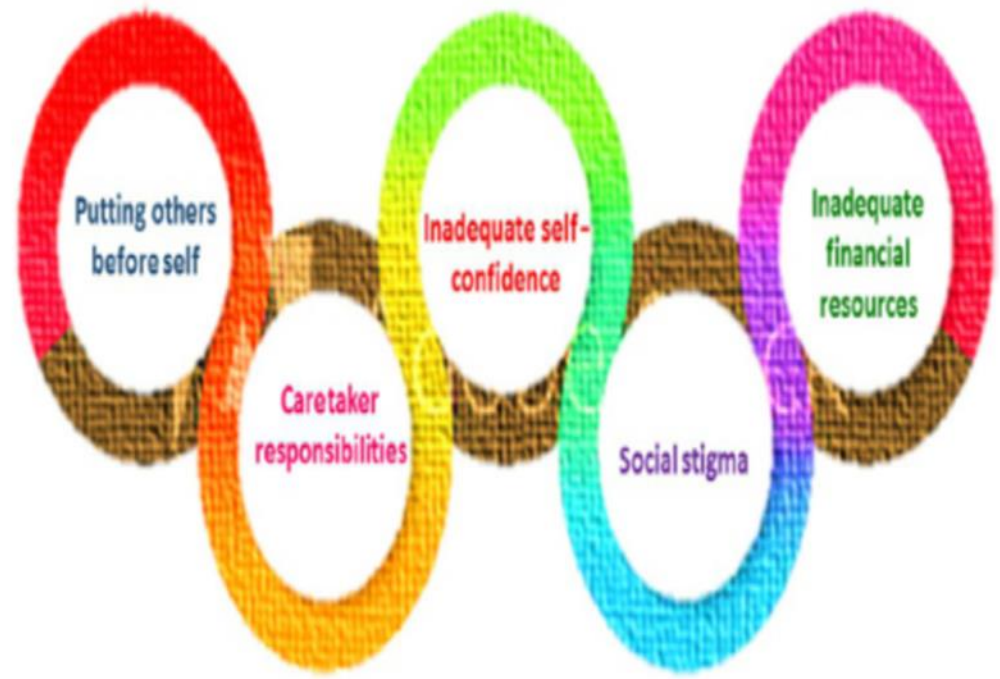
**Socioeconomic**



Unhealthy



Congenital heart disease



Stress and social isolation

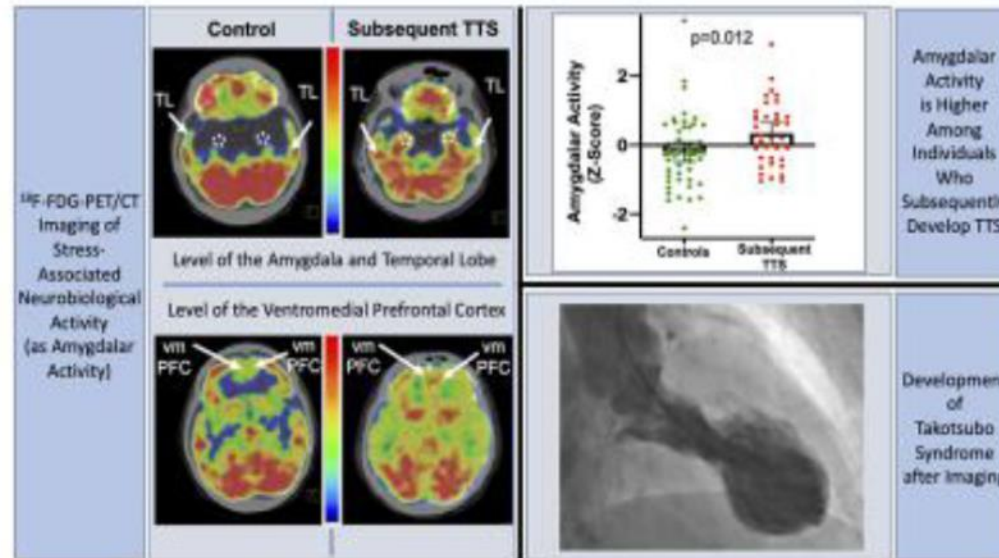


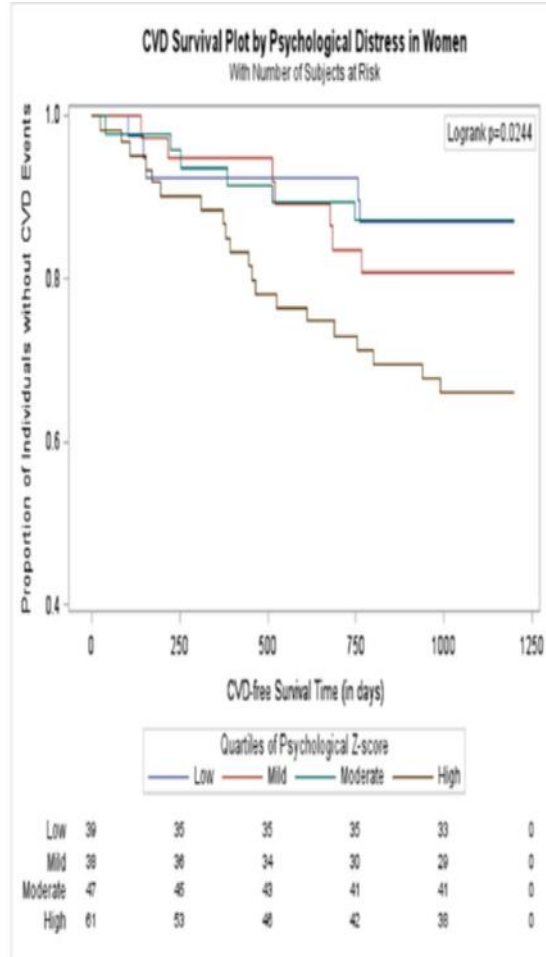
- Coronary artery disease
- Heart failure
- Dementia
- Metabolic syndrome
- Atrial fibrillation
- Peripheral artery disease
- Stroke
- Cancer treatment associated heart disease
- HFpEF > HFrEF

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].*

# 9. Con in the Cardio

Relationship between stress-associated neurobiological activity on  $^{18}\text{F}$ -FDG-PET/CT imaging and risk ...





After diagnosis of CAD psychological distress associated higher risk of events in women compared to men

Greater vulnerability to psychological stress  
Psychosocial stress increases risk of CVD generally

Current system ill-equipped to provide integrated comprehensive care to women and men with heart disease

(Pimple JAHA 2019, Rosengren and Manheim, 2015)



# Spectrum of IHD

## Key sex differences in acute coronary syndromes and ischemic heart disease



- Compared to men, women are less likely to undergo angiography, undergo PCI, or receive guideline-directed medical therapy
- Women are more likely to experience:
  - Myocardial infarction with non-obstructive coronary arteries (MINOCA)
  - Spontaneous coronary artery dissection (SCAD)
  - Takotsubo cardiomyopathy
- Women are more likely to have coronary microvascular dysfunction

8

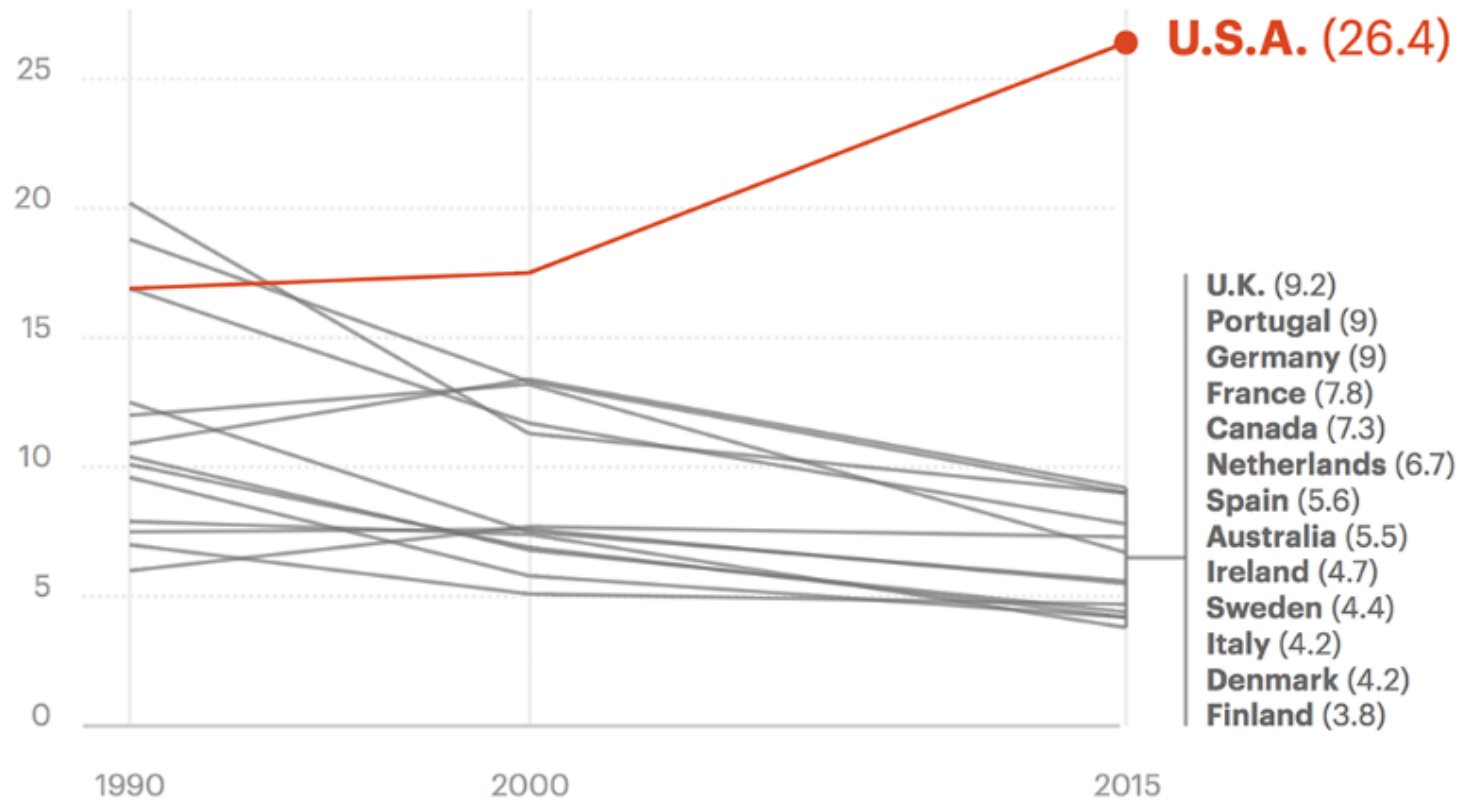
Need to develop effective prevention, diagnosis, and treatment approaches

# CARDIOVASCULAR DISEASE AND PREGNANCY

- Cardiovascular disease is a major contributor to (late) maternal death worldwide.
- Late maternal death is not well documented and therefore, a neglected issue.
- Data on pregnancy outcomes in women with uncorrected congenital heart disease are very limited. Studies and registries addressing these knowledge gaps are urgently needed.
- Cardio-Obstetrics is an emerging multidisciplinary team approach and crucial for optimal care for women with cardiovascular disease during pregnancy.
- Prevalence of rheumatic heart disease remains high in certain regions of the world, and young women of childbearing age are disproportionately affected.
- Multidisciplinary cooperation combined with appropriate pre-conception counselling and antenatal care is crucial to reduce complications from rheumatic heart disease in pregnancy.

# Maternal Mortality is Rising in the US as it Declines Elsewhere.

Deaths per 100,000 live births



## Notes

"Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015," *The Lancet*. Only data for 1990, 2000 and 2015 was made available in the journal.

# Racial/ethnic Disparities in Pregnancy-Related Mortality

The New York Times

*For Serena Williams, Childbirth Was a Harrowing Ordeal. She's Not Alone.*



After giving birth in September, Serena Williams was bedridden for six weeks from a string of medical complications. Martin Dokoupil/European Pressphoto Agency

Deaths per 100,000 live births

42.8 black non Hispanic

32.5 American  
Indian/Alaskan native

13.0 white non Hispanic

14.2 Asian/Pacific islander  
non Hispanic

11.4 for Hispanic women



# Why is Maternal Mortality Increasing?

- Women are older, more chronic conditions
- Fertility Therapies → greater incidence of multiple gestation pregnancies
- Lack of access to primary care
- Variability in quality of care
- Lack of national protocols and thus standardized care
- Lack of systemic review of cases
- Rising rate of Caesarian section
- Variable access to birth control – which allow a pregnancy to be planned and preexisting medication conditions are optimally managed

# 4 Key Factors Related to Maternal Cardiovascular Mortality

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 212

- Race/Ethnicity
  - Black women have 3.4 times risk of dying than whites
- Age
  - Age >40 increases risk to 30 TIMES the risk of women <20 years old
- Hypertension – chronic or hypertensive disorder of pregnancy
  - Risk of MI is 13 fold
  - Risk of heart failure is 8 fold
- Obesity
  - 60% of maternal deaths occur in overweight or obese women

# Sex-specific Questionnaires – You gotta ask!

MASSACHUSETTS GENERAL HOSPITAL  
CORRIGAN MINEHAN HEART CENTER  
Elizabeth Anne and Karen Barlow Corrigan Women's Heart Health Program  
Tel: 617-643-3400 | Fax: 617-643-0192

Diabetes  
If you have relatives with diabetes, which \_\_\_\_\_  
Yes No  
(that applies)

Have you ever been pregnant?  
If yes, how many pregnancies have you had? \_\_\_\_\_  
If yes, how many live births have you had? \_\_\_\_\_

Did you have high blood pressure before pregnancy?  
If yes, before how many pregnancies? \_\_\_\_\_

Did you have pre-eclampsia or eclampsia?  
Did you deliver before the 37th week of pregnancy?  
If yes, before you many pregnancies? \_\_\_\_\_

Did you deliver before the 34th week of pregnancy?  
If yes, before you many pregnancies? \_\_\_\_\_

Were there problems with growth of the fetus during your pregnancy?  
If yes, before you many pregnancies? \_\_\_\_\_

Was your baby small for her/his age at birth?  
If yes, before you many pregnancies? \_\_\_\_\_

Did you have diabetes before the start of pregnancy? Yes No  
If yes, before you many pregnancies? \_\_\_\_\_

Did you develop diabetes during pregnancy? Yes No  
If yes, before you many pregnancies? \_\_\_\_\_

Did you have heart failure prior to your first pregnancy? Yes No  
If yes, before you many pregnancies? \_\_\_\_\_

Did you develop onset of heart failure during pregnancy? Yes No  
If yes, before you many pregnancies? \_\_\_\_\_

Have you ever had a miscarriage? Yes No

Did you have a hysterectomy or surgical removal of ovaries, why \_\_\_\_\_  
Related to chemotherapy

Are you currently taking hormone replacement therapy (HRT)? Yes No

Have you ever been on hormone replacement therapy (HRT)? Yes No  
At what age did you stop HRT? \_\_\_\_\_  
How many years did you take HRT? \_\_\_\_\_

Please list any natural supplements you are taking or have taken (ex. St. John's Wort, black cohosh, plant based estrogens)? \_\_\_\_\_

MEDICATIONS

Do you have any medication allergies? NO YES (please describe)

Leverage the power of the EHR but you must make sure the important data is entered into the EHR up front

# Comprehensive CVD Prevention and Care



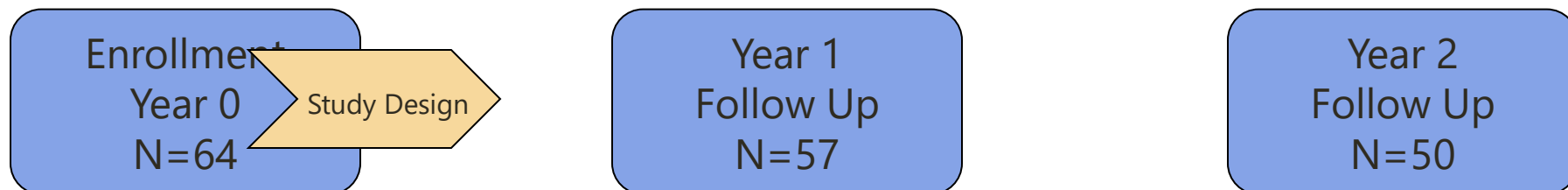
**FIGURE 3** Nonpharmacologic and Pharmacologic Approaches to Addressing CVD in Men and Women. ASCVD, atherosclerotic cardiovascular disease.

# Heart Awareness and Primary Prevention in Your Neighborhood

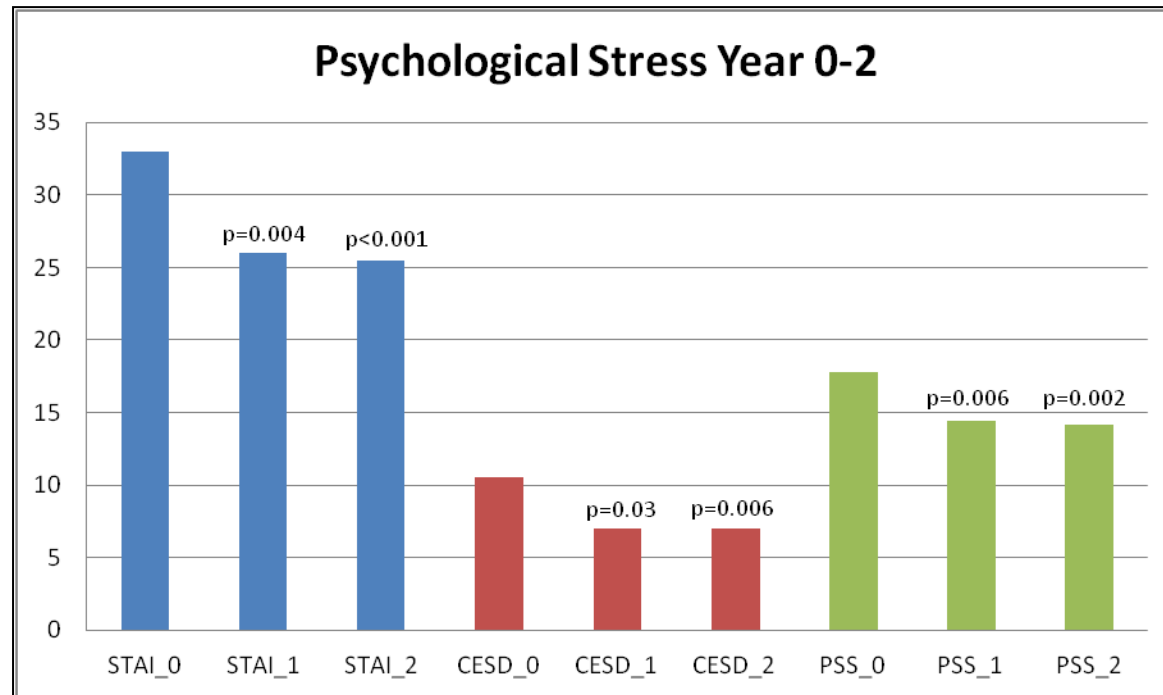
- Unique heart disease prevention model
- Low income women, 40-60 years of age
- Integration of individual and group health education/coaching, exercise, nutrition and stress management in a community health center

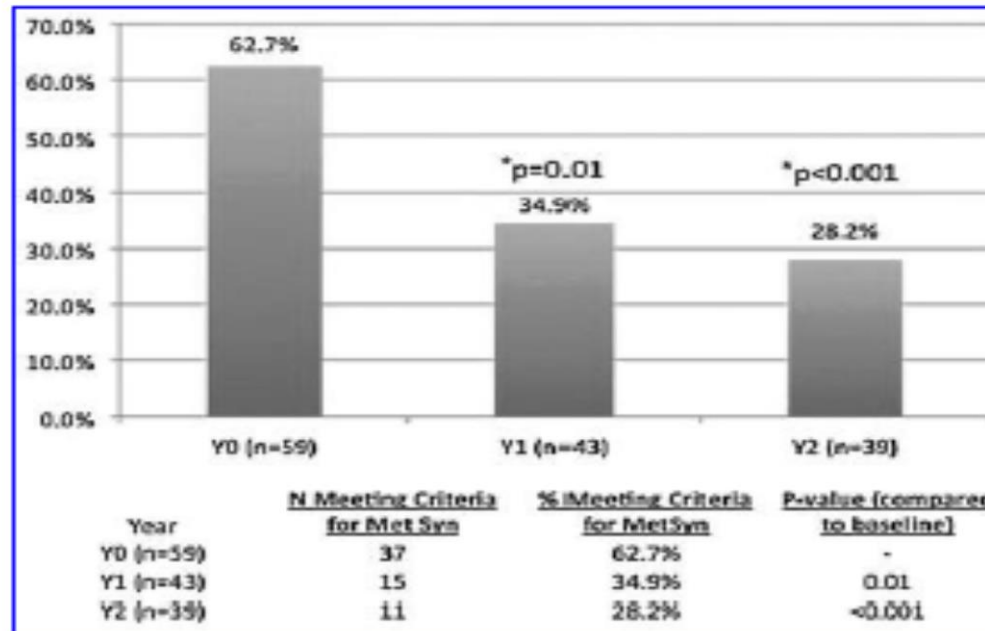
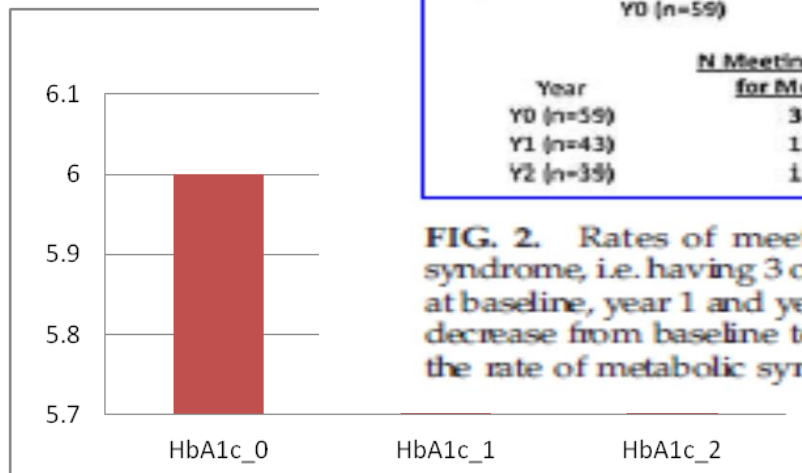
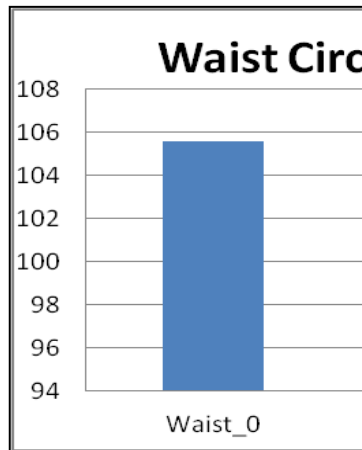
# Methods: Study Design

Exercise	Nutrition	Psychological	Smoking
PT Consult ↓ Individualized exercise plan ↓ Regular check in w/ Health Coach	Nutrition Consult ↓ Individual diet - Cost/Family ↓ Regular check in w/ Health Coach	CESD-10 STAI PSS ↓ HAPPY Heart Relaxation & Medication Classes ↓ Regular check in w/ Health Coach	Offered cessation program  Offered free pharmacologic options
*HAPPY Heart Exercise Classes	*HAPPY Heart Cooking Classes		



# Happy Heart Approach





**FIG. 2.** Rates of meeting diagnostic criteria for metabolic syndrome, i.e. having 3 of 5 components of metabolic syndrome, at baseline, year 1 and year 2. This figure displays the significant decrease from baseline to year 1 and from baseline to year 2 in the rate of metabolic syndrome. \*Denotes significant value.



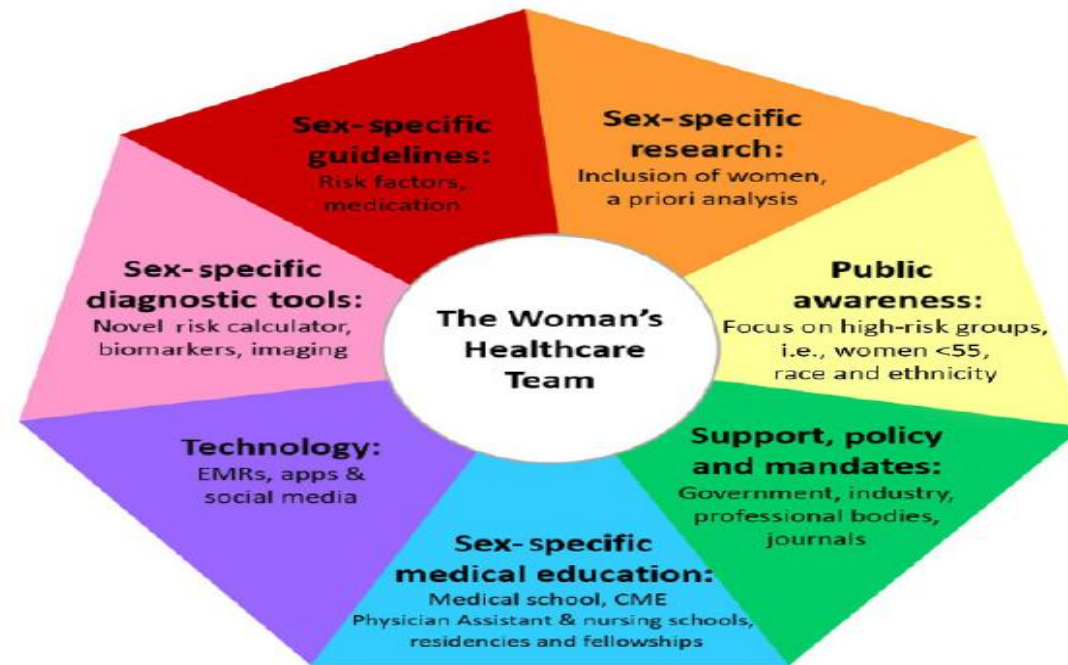
# Global Burden of CVD in Women-

## Key Points

- Cardiovascular disease remains the leading cause of death in women worldwide
- With regard to CVD subtypes, ischemic heart disease is the most common cause of CVD death worldwide
- A global approach to education, screening and treatment of women is warranted
- Women have unique risk factors for heart disease across their lifespan
- Reproductive history is important for early prevention and treatment of CVD
- Psychological health and wellbeing are essential for CVD risk mitigation

- Sex and gender disparities in outcomes persist, particularly in women disadvantaged by race, ethnicity, income level or educational attainment
- Sex specific impact of novel and traditional risk factors should be included for improved risk stratification in women
- Optimal CV care involves partnerships among women, their communities and the academic and community-serving health systems that engage in strategic planning to redesign care to meet the needs of diverse groups of women

# Solutions for Equitable Care for Women



**FIGURE 5** Contemporary Solution for Equitable Care and to Improve Cardiovascular Outcomes in Women. CME, continuing medical education; EMRs, electronic medical records. *Adapted with permission from [67].*

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