CARDIOVASCULAR DISEASE IN WOMEN

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OBJECTIVES

At the conclusion of this presentation attendees will be able to:

1. Define and discuss the 4 major categories of cardiovascular disease and the 10 risk factors.
2. List 3 major pregnancy complications of CVD and discuss the prevalence of CVD and incidence in women.
3. List 10 lifestyle choices to protect the heart.

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TYPES OF CVD

- Types of CVD (WHO)
  - Coronary Heart Disease-caused by epicardial coronaries
  - Stroke-ischemic or hemorrhagic process occurring in brain
  - Other cardiovascular Dz-tumors, cardiomyopathy, valve dz, amyloids, restrictive/constrictive CM, vascular diseases –PVD, DVT, PE
  - Hypertensive Heart Disease-AAA, CM
  - Inflammatory heart disease-Sarcoidosis, trauma, toxins, ETOH
  - Rheumatic Heart disease-caused by rheumatic fever –mitral valve diseases etc.

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RISK FACTORS-WOMEN

NON-TRADITIONAL FACTORS
- Hypertensive disorders
- Metabolic disorders of pregnancy
- Early Menopause
- Surgical Menopause
- Early Menarche
- Pre-term delivery
- Depression
- Breast Cancer Treatment

TRADITIONAL FACTORS
- Age
- Hypertension
- Dyslipidemia
- DM
- Obesity
- Cigarette smoking
- Family History of CVD

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WHAT IS CARDIOVASCULAR DISEASE

- What is the difference between CAD and IHD (ischemic heart disease)
  - CAD specifically refers to disease of the epicardial coronaries
  - IHD disease of coronary arteries, microcirculation, and from supply demand inequities (example)
  - IHD causes-Microvascular dysfunction, coronary reactivity, plaque erosion/distal microembolization
  - Differences in presentation, frequency, quality of CVD between women and men originate from gene and hormone expression.

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CVD- CONT.

- CVD is the leading cause of death in women worldwide, disproportionately affecting low and middle income countries
- 32% deaths women US (>450,000) due to CVD
- Pre-menopausal woman age >40 similar to risk of men at age 30
- Women present later (10years) , experience more complications and worse outcomes
- Unlike breast cancer, heart disease comes quickly and kills more frequently
- What do you feel is the #1 modifiable risk factor for women, esp age<50?

Shah et al. Gender differences, symptom evaluation, and diagnostic strategies. JACC. (2006), 47(3)

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CVD-CONT.

- DM is weighted higher risk factors for women than men
- Emotional stress at work or home portends poor outcome in healthy women and those with CAD (emotional stress can trigger coronary event)
- Unique risk factors –low estrogen, elevated testosterone, polycystic ovarian syndrome, Elevated C-Reactive protein, Pregnancy

Shah et al. Gender differences, symptom evaluation, and diagnostic strategies. JACC. (2006). 47(3)

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ISCHEMIC HEART DISEASE

- Delay in diagnosis is delayed care-atypical symptoms mostly contributed to ?
- Yentl syndrome-if you are a male that presents with symptoms you get the care, since women don't look like men –less likely to have heart disease go as a differential
- Misinterpretation of symptoms
- STEMI "Men explode women implode"-Women have more microvascular Dz and endothelial dysfunction, reduced coronary flow not seen on cath. Men have more obstructive
- Women<55 with ACS at higher risk for SCD.

Garcia et al. Cardiovascular disease in women clinical perspective Circ Res. 2016;118:1273-1293.DOI: 10.1161/CIRCRESAHA.116.307547

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ISCHEMIC HEART DISEASE CONT.

- Delay in seeking care, takes longer to diagnose and less likely to refer women for stress testing
- ACS portends (10.2% vs 5.5%) higher mortality in women than their male counterparts
- Most research studies for ACS based on which medications are approved have included men
- Women with non-obstructive Dz benefit more from BB than Calcium Channel Blocker
- ACEI and Statins can help to relieve symptoms –microvascular dz
- Less likely to get aspirin

Garcia et al. Cardiovascular disease in women clinical perspective Circ Res. 2016;118:1273-1293.DOI: 10.1161/CIRCRESAHA.116.307547

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CORONARY MICROVASCULAR DYSFUNCTION

- Limited coronary flow reserve and **coronary endothelial dysfunction** –increased rates of death, stroke or heart failure.
- Smaller epicardial coronaries, diffuse atherosclerotic disease, increased arterial stiffness, fibrosis, altered remodeling and the **presence of endothelial** or smooth muscle dysfunction
- Invasive coronary vasomotor testing-done using Acetylcholine. In a study of 1,379 patients with stable angina and un-obstructive CAD, ACH was administered.
  - Pathological test was found in women>men (70% vs 43%) Vasomotor dysfunction occurred at lower dosages in females than males

Garcia et al. Cardiovascular disease in women clinical perspective. Circ Res. 2014;118:1273–1293. DOI: 10.1161/CIRCRESAHA.116.307547

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Table 3. Risk-Enhancing Factors for Clinician-Patient Risk Discussion **ACC/AHA SLIDE**

Risk-Enhancing Factors
• **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
• **Primary hypercholesterolemia** (LDL-C 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
• **Metabolic syndrome** (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [>150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
• **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
• **Chronic inflammatory conditions,** such as psoriasis, RA, lupus, or HIV/AIDS

ABI indicates ankle-brachial index; AIDS, acquired immunodeficiency syndrome; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.

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Table 3. Risk-Enhancing Factors for Clinician-Patient Risk Discussion (cont'd). ** ACC/AHA SLIDE**

Risk-Enhancing Factors
• **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
• **High-risk race/ethnicity** (e.g., South Asian ancestry)
• **Lipids/biomarkers**: associated with increased ASCVD risk, ↑ Triglycerides (≥175 mg/dL, nonfasting);
• **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
• **Elevated Lp(a):** A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
• **Elevated apoB** (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
• **ABI** (<0.9)

*Optimally, 3 determinations.

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RISK FACTORS AND THEIR IMPACT

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DIABETES

- Detrimental effect of glucose occur at lower glycemic levels below threshold for diagnosis- impact of formal diagnosis is more detrimental since subclinical impact has been occurring for months-years before diagnosis
- Hence metabolic and vascular risk factor profile in pre diabetic > in women than men
- Impaired endothelium-dependent vasodilation (Inflammatory condition)
- Hypercoagulable state
- Atherogenic dyslipidemia
- Metabolic syndrome
- Elevated inflammatory markers- hsCRP, IL-6 and TNF α

Inflammation, depression and cardiovascular disease in women: the role of the immune system across critical reproductive events. Therapeutic Advances in Cardiovascular Disease May 2019. doi: 10.1177/1753944719851903

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SMOKING /OBESITY AND OVERWEIGHT

- Major thing to remember—impact of smoking and oral contraceptive has "synergistic" impact on AMI, stroke and Venous Thromboembolism
- 2/3 adults are overweight or obese, women>men
- Framingham study confers- 64% with increased the risk of CAD
- Increase inflammatory markers of CRP, IL 1 β, TNFα, Leptin noted in obese women
- Physical inactivity linked to high hsCRP is prevalent-increased with age (has inverse relationship with ASCVD)
  - Recommendation of 150minutes/week of moderate intensity aerobic activity or 75 minutes of vigorous activity
  - Anaerobic activity >2hours/week
  - Physical Activity reduces inflammation

Moreno, G. et al. Inflammation, C-reactive protein, and cardiovascular disease in women at the end of the reproductive period across critical reproductive events. Therapeutic advances in cardiovascular disease (2019). https://journals.sagepub.com/doi/10.1177/1753944719851903

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OBESITY STATISTICS 1963-202

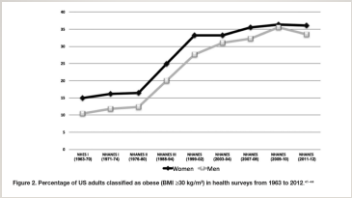

Figure 2. Percentage of US adults classified as obese (BMI ≥30 kg/m²) in health surveys from 1963 to 2012.[47,48]

Garcia et al. Cardiovascular disease in women: clinical perspective Circ Res. 2016;118:1273-1293. DOI: 10.1161/CIRCRESAHA.116.307547

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HYPERTENSION

- Physiologically endogenous estrogen maintain vasodilation and maintain BP control
- Post menopausal increase of BP
- RCT-Systolic BP Intervention Trial (SPRINT)-SBP>130 and increased CVD risk randomized to intensive treatment goal <120 or standard treatment goal <140
- Intensive treatment resulted in 25% lower relative risk of MACE and overall deaths
- Inflammatory markers-PE during pregnancy linked to IL6, TNFα, and RAAS system

Inflammation, depression and cardiovascular disease in women: the role of the immune system across critical reproductive events. Therapeutic Advances in Cardiovascular Disease May 2019. doi: 10.1177/1753944719851950

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DYSLIPIDEMIA

- Highest impact on women post menopause
- Dyslipidemia pre- menopause ASCVD not observed
- Lifestyle modification-diet and exercise of most importance
- Pharmacological therapy important in primary and secondary prevention
- Primary prevention is sex-specific now with AHA/ACC-more women will qualify for treatment with statins
- 45% of those additional eligible women inspite of guidelines are not prescribed statins
- controversy surrounding statins may place women at risk for DM needs exploration
- Advanced lipid testing with Lp-PLA2 (lipoprotein-associated pholipase A2) predicting ASCVD may play a role

Garcia et al. Cardiovascular disease in women clinical perspective Circ Res. 2016;118:1273-1293. DOI:

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NON TRADITIONAL ASCVD FACTORS- PREGNANCY AND CVD

- Pregnancy- considered a "stress test" for CV system. Can cause Hypertension and Metabolic disorders- independent risk factors for CVD
- Gestational HTN: SBP>140/90 after 20 weeks of pregnancy
- Chronic HTN: SBP>160/110 less than 20 weeks of pregnancy; greater risk for preeclampsia
- Pre-eclampsia (PE)
  - New onset of HTN >20weeks of gestation with e/o proteinuria (0.3g/24h) and or AKI, liver dysfunction, neurological involvement, thrombocytopenia, hemolysis, or fetal growth restrictions

Women and CV Dz: Pregnancy, the forgotten risk factor https://doi.org/10.1016/j.hlc.2019.09.011

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PRE-ECLAMPSIA AND CVD

- Systematic search –Medline and Embase
- 22 studies identified with >6.4 million women, 250,000 with PE
- Pre-Eclampsia was independently associated with increased risk of future Heart Failure (RR4.19; 95% Confidence Interval)2.09-8.13, CAD (RR 2.50; 95% CI, 1.83-2.66 and Stroke (RR 1.81; 95% CI, 1.29-2.55)
- Conclusion-PE associated with 4-fold increase in risk of HF, 2-fold increase CAD, Stroke, and Death
- Permanent endothelial dysfunction with increase risk of future CVD; Inflammation and RAAS linked to PE

Preeclampsia and Future Cardiovascular Health: https://doi.org/10.1161/CIRCOUTCOMES.116.003497

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CHAMPS STUDY & NURSES HEALTH STUDY

- Included: >1 million women
- Those with PE had 2x risk of developing CVD (HR 2.0 CI 95% 1.7-2.2)
- Those with PE and Metabolic Syndrome had 12 fold increase in CVD (HR 11.7, 95% CI 4.9-28.3)
- Co-Existence PE and poor fetal growth –increased maternal mortality hazard ratio compared to PE alone
- Gestational Diabetes-leads to onset of DM within 5-10years of post partum
- NHS: 43% increased risk of MI or stroke post GDM

Arnott C, et al. Women and Cardiovascular Disease: Pregnancy, the Forgotten Risk Factor. Heart, Lung and Circulation (2019), https://doi.org/10.1016/j.hlc.2019.09.011

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NON TRADITIONAL ASCVD FACTORS- GESTATIONAL DIABETES

- Due to epidemic of obesity-increased number of women found to have DM in 1st trimester- T2DM
  - 7-fold increased risk for DM; 2-fold increase of stroke and 4-fold for MI (5-10years post partum)
- Eclampsia and gestational diabetes (GDM)
  - Glucose intolerance with plasma glucose diagnostic criteria fasting, 1- and 2- hour
- Hypertensive Disorder of Pregnancy –represents conditions characterized by endothelial dysfunction/vascular function in early adulthood (portend early CVD)
- Inflammatory markers- hsCRP, IL6, and TNF α implicated in GD

Arnott C, et al. Women and Cardiovascular Disease: Pregnancy, the Forgotten Risk Factor. Heart, Lung and Circulation (2019), https://doi.org/10.1016/j.hlc.2019.09.011

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NON TRADITIONAL ASCVD FACTORS-

PRE-TERM DELIVERY

- Defined as delivery <37 weeks gestation
- Underlying causes not well understood-felt to be due to inflammation, infection, vascular Diseases
- PTD is noted to be an independent risk factor for CV morbidity and CV related hospitalizations

WEIGHT GAIN -PREGNANCY

- Body weight increases by 20%
- Reduced weight post pregnancy-breast feeding, normalized eating habits, exercise, sleep disturbance
- Weight at 1 year portends likelihood of being overweight 15years later

Arnott C, et al. Women and Cardiovascular Disease: Pregnancy, the Forgotten Risk Factor. Heart, Lung and Circulation (2019), https://doi.org/10.1016/j.hlc.2019.09.011

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AUTOIMMUNE DISEASE

RA AND SLE

- Association between inflammatory dz and increased mortality-CVD
- Self-antigen results in tissue destruction
- Microvasculature plays a role in predisposition of women with RA/SLE to develop ASCVD
- RA-3 fold increase in MI; 50% risk stroke
- SLE 9-fold MI; 50 fold increased stroke

RADIATION/CHEMOTHERAPY

- Radiation therapies –for breast cancer inadvertently damage heart-cause cardiomyopathy, valve dz
- Research suggests radiation to Lt breast with greater incidence of CAD events-esp with predisposing risk factors
- Type-I (anthracycline-like) or Type-II (Trastuzumab-like) evidence of cardiotoxicity

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MENOPAUSE

- Estradiol exposure during reproductive events control inflammatory response
- Estradiol influences cytokine secretion and reduced expression of IL-6, increased production of anti-inflammatory IL-10
- Known that early Menarche and menopause linked to CVD risk.
- Changes to the fluctuation of estrogen and progesterone can impact immune system (trigger CVD and depression)
- Lack of Estradiol causes pro inflammatory state leading to CVD

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SPONTANEOUS CORONARY ARTERY DISSECTION

- Sudden separation of layers of coronary artery wall-causing hematoma
  - Obstructs intraluminal blood flow resulting in MI
  - Occurs in 25% of women in peripartum; average age is 42
  - Presentation-young woman without risk factors with sudden onset of ACS
  - Maybe a genetic predisposition
  - Accurate diagnosis is a must since traditional PCI is less successful, there is spontaneous healing hence conservative management
  - Statins are discouraged some association with statins. Use only if there is hyperlipidemia

Gluckman et al. Cardiovascular disease in women: clinical perspective Circ Res. 2014;114:1376-1397. DOI: 10.1161/CIRCRESAHA.114.302547

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TAKOTSUBO SYNDROME-STRESS CARDIOMYOPATHY

- Transient LV systolic and diastolic dysfunction with SWMA
- Affects post menopausal women and follows period of extreme physical and emotional stress
- Clinical presentation similar to ACS, coronary anatomy without obstructive Dz
- Exact etiology unclear-may be related to disproportionate distribution of sympathetic receptors. Ventricular Fx improves with supportive therapy

Kaseqe-Arachi, T. & Sharma, S. Cardiovascular disease in women: Understanding symptoms and risk factors. European Cardiology Review 2017; 12(1): 10.15420/ecr.2016:32:1

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HEART FAILURE IN WOMEN

- Women suffer from HFpEF EF>52%, most likely due to diastolic dysfunction
- Limited LV systolic reserve, systemic and pulmonary vascular function, coronary microvascular endothelial inflammation and reduction of nitric oxide bioavailability, right heart function, left heart function, autonomic tone
- Treatment-Beta blockers to increased LV diastolic filling time
- Peripartum Cardiomyopathy-develops during or post partum without CVD, 1-3000 deliveries, increased incidence in AA women, >30years, Pregnancy assoc. HTN
- Most women demonstrate recovery 2-6 months post diagnosis

Gucia et al. Cardiovascular disease in women: clinical perspective Circ Res. 2014;114:1278-1293. DOI: 10.1161/CIRCRESAHA.114.302547

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STROKE

- 53% of women have strokes annually– approx. 55,000 more strokes than men
- Meta-analysis 4, 371, 714 AF was a strong risk factor for stroke in women more than men
  - Also associated with higher all cause mortality, CV death, CV events, heart failure
  - Routine screening for AF in women >75 using VS and auscultation
  - AC should be offered using CHA2D2 VASc score
- PAD portends equal morbidity and mortality to CAD and stroke
  - Intermittent claudication-ABI can be done
  - Screening to be done >65 or for Hx of tobacco or DM

Gucia et al. Cardiovascular disease in women: clinical perspective Circ Res. 2014;114:1278-1293. DOI: 10.1161/CIRCRESAHA.114.302547

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ABDOMINAL AORTIC ANEURYSMS

- AAA more common in men than women
- Women with AAA also portend poorer prognosis
- Meta-analysis showed annual risk of rupture AAA >5.0cm is 18%

Gucia et al. Cardiovascular disease in women: clinical perspective Circ Res. 2014;114:1278-1293. DOI: 10.1161/CIRCRESAHA.114.302547

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AUTO-IMMUNE DISORDERS

- Patients with Auto-immune disorders especially those who have undergone radiation and or chemotherapy-recommended for long-term surveillance program
- Echocardiographic associations, American and European recommend evaluation based on symptoms and echo findings to continue surveillance 5years and high risk 10years post completion of therapies

Gunca et al. Cardiorespirat. disease in women: Historical perspective Circ Res. 2016;118:1291. DOI: 10.1161/CIRCRESAHA.116.307547

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DEPRESSION AND CVD

- Chronic inflammation exists in depression and CVD
- Midlife those diagnosed with Major Depression disorder have 2x more CVD events
- Imbalance of Hypothalamus-pituitary-adrenal (HPA) axis, RAAS, Serotonin/Kynurenine pathways
- All above cause inflammation and endothelial dysfunction
- Changes to inflammatory cytokines in relation to hormonal fluctuation associated with reproductive events (menstrual cycle/perinatal period/menopause)

Inflammation, depression and cardiovascular disease in women: the role of the immune system across critical reproductive events. Therapeutic Advances in Cardiovascular Disease May 2019. doi: 10.1177/1753944719851950

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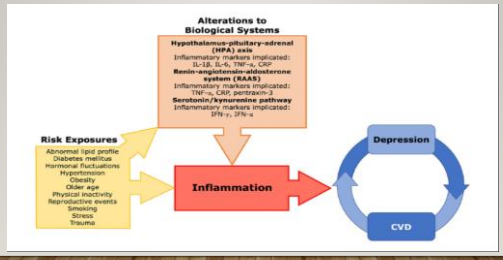
DEPRESSION



Inflammation, depression and cardiovascular disease in women: the role of the immune system across critical reproductive events. Therapeutic Advances in Cardiovascular Disease May 2019. doi: 10.1177/1753944719851950

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INFLAMMATION

- Measuring cytokine level can provide input into inflammatory response
- Level of cytokine and IL6 are elevated in individuals with depression and also in individuals with CVD
- Higher CRP levels are noted in women with CVD. If CRP is elevated without CVD, it is found to be related to higher BMI, HTN, and smoking
- TNF α elevated in CHF patients <50, post this it rises sharply, stays steady in men → likely related to hormonal changes
- RAAS system-linked to activation by inflammation-increased aldosterone noted in depression.

Inflammation, depression and cardiovascular disease in women: the role of the immune system across critical reproductive events. Therapeutic Advances in Cardiovascular Disease May 2019. doi: 10.1177/1753944719851950

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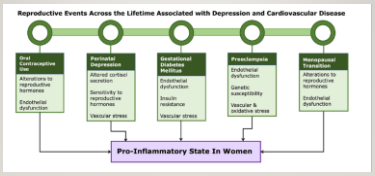
REPRODUCTIVE EVENTS AND INFLAMMATION



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LETS TALK PREVENTION

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PRIMARY PREVENTION GUIDELINES

- Smoking cessation
- Healthy body weight (BMI<25)
- Healthy diet
- Exercising
- No more than moderate amount of alcohol
- INTERHEART Study-52 countries large case-control study screened patients post first MI
  - 9 risk factors identified-smoking, lipids, HTN, DM, obesity, diet, physical activity, alcohol, psychosocial factors) found to be 90% attributed to MI

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TABLE 8. HIGHLIGHTS OF RECOMMENDED BEHAVIORAL AND PHARMACOTHERAPY TOBACCO TREATMENT MODALITIES ACC/AHA SLIDE*

Timing of Behavioral Interventions†		
<3 min of tobacco status assessment with cessation counseling at each clinic encounter	>3-10 min of tobacco status assessment with cessation counseling at each clinic encounter	>10 min of tobacco status assessment with cessation counseling at each clinic encounter

** COPIED FROM ACC/AHA**
†Timing of assessment relates to ICD-10 coding.

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TABLE 8. HIGHLIGHTS OF RECOMMENDED BEHAVIORAL AND PHARMACOTHERAPY TOBACCO TREATMENT MODALITIES (CONT'D) ACC/AHA SLIDE*

Treatment	Dosing‡		Precautions
NRT*			
Patch	21 mg, 14 mg, or 7 mg	Starting dose: 21 mg for >10 CPD; 14 mg for <10 CPD	Local irritation possible; avoid with skin disorders; may remove for sleep if needed
Gum	2 mg or 4 mg	Starting dose: 4 mg if first tobacco use is ≤30 min after waking; 2 mg if first tobacco use is >30 min after waking; maximum of 20 lozenges or 24 pieces of gum/d. Chew and park gum*	Hiccups/dyspepsia possible; avoid food or beverages 15 min before and after use
Lozenge	2 mg or 4 mg		

*FDA can guide dosing. 1 CPD 1–2 mg of nicotine. Note: Use caution with all NRT products for patients with recent (≤2 wk) MI, serious arrhythmias, or angina, patients who are pregnant or breastfeeding, and adolescents.

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TABLE 8. HIGHLIGHTS OF RECOMMENDED BEHAVIORAL AND PHARMACOTHERAPY TOBACCO TREATMENT MODALITIES (CONT'D) ACC/AHA SLIDE*

Treatment	Dosing‡		Precautions
NRT*			
Nasal spray	10 mg/mL	Starting dose: 1-2 doses/h (1 dose=2 sprays); maximum of 40 doses/d	Local irritation possible; avoid with nasal or reactive airway disorders
Oral inhaler	10, 10-mg cartridge	Starting dose: Puff for 20 min/cartridge every 1-2 h; maximum 6-16 cartridges/d; taper over 3-6 mo§	Cough possible; avoid with reactive airway disorders

*CPD can guide dosing. 1 CPD is ≈1-2 mg of nicotine. *Note: Use caution with all NRT products for patients with recent (≤2 wk) MI, serious arrhythmia, or angina; patients who are pregnant or breastfeeding; and adolescents.*

‡Dose and duration can be titrated on the basis of response

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TABLE 8. HIGHLIGHTS OF RECOMMENDED BEHAVIORAL AND PHARMACOTHERAPY TOBACCO TREATMENT MODALITIES (CONT'D) ACC/AHA SLIDE**

Treatment	Dosing‡		Precautions
Other‖			
Bupropion (Zyban [GlaxoSmithKline], Wellbutrin SR [GlaxoSmithKline])	150 mg SR	150 mg once daily (am) for 3 d; then 150 mg twice daily; may use in combination with NRT (S4.5-21)	Avoid with history/risk of seizures, eating disorders, MAO inhibitors, or CYP 2D6 inhibitor
Varenicline (Chantix [Pfizer])	0.5 mg or 1 mg	0.5 mg once daily (am) for 3 d; then 0.5 mg twice daily for 4 d; then 1 mg twice daily (use start pack followed by continuation pack) for 3-6 mo	Nausea common; take with food. Renal dosing required. Very limited drug interactions; near-exclusive renal clearance.

‡Dose and duration can be titrated on the basis of response

§See Rx for Change for greater detail: http://rxforchange.ucsf.edu)

‖The FDA has issued a removal of black box warnings about neuropsychiatric events and initiation, morning; CPD, cigarettes smoked per day; FDA, U.S. Food and Drug Administration; ICD-10, International Classification of Diseases, Tenth Revision; MAO, monoamine oxidase; NRT, nicotine replacement; and SR, sustained release.

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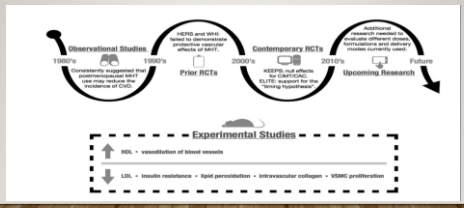
MENOPAUSAL HORMONE THERAPY TIMELINE



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MENOPAUSE AND MENOPAUSE HORMONE THERAPY

- Ovarian sex hormone, estrogen is cardio protective-Initial studies were observational studies. Prospective studies refute this conclusion
- Women's Health Initiative and Heart Estrogen/Progestin Replacement Study (HERS) - based on study findings there was decline in Menopause hormone therapy
- Critical evaluation of trials along with another meta-analysis >39,000 women 23 trials concluded that hormone therapy reduces CAD risk for women<60years of age.
- Consensus is to prescribe HRT at lowest effective dosage for menopausal symptoms in early menopause (approx. 5years), NEVER FOR PREVENTION OF CVD

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BCRA CARRIERS, PROPHYLACTIC SLO, AND MENOPAUSE

- Positive BCRA or BCRA2 greater elevated lifetime risk of ovarian, fallopian, breast cancer
- SLO-prophylactic recommended often before natural menopause, to prevent cancer
- Increased risk of premature CVD
- No guidelines for above
- Short term HRT, osteoporosis prevention, and possible effect on cognition

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ASPIRIN

- Women's Health Study (WHS) 40,000 women >45years old on low dose asa 100mg or placebo for 10years
  - Statistically non significant reduction in primary composite outcome
  - Asa significantly lowered risk of stroke by 17%, increased risk of GIB
  - Did not lower the risk of MI or CV death (opposite effect of asa in men)
  - Subgroup analysis revealed benefit>risk >65years or age for primary prevention of both MI and Stroke (class IIa level of evidence B); (must be given to those with controlled HTN). Maybe reasonable for those <65 (class IIb level of evidence B)
- ASA and DM-controversial-Acc to ADA low dose ASA should be considered for those with 10year risk of 10% or more (not at increased risk for bleeding +>60+at least 1 risk factor)
- ASA should NOT be recommended for adults with DM and low risk men<50 and women<60 & no CVD risk factors

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STATINS

- ACC/AHA guidelines revised to reduce ASCVD in adults with MI-moderate to high dosage of statins
- There is proportional reduction of CV event for every 1.0mmol/L LDL reduction.
- Those between 40-75 without CVD treat with statin for LDL>189;if with DM treat with moderate to high dosage of statins based on 10-year ASCVD risk
- If the 10-year ASCVD risk is >7.5% moderate to high dosage statin only after discussion regarding patient risk benefit to address other risk factors and optimized lifestyle is discussed and implemented.
- Fixed dosage of statins without testing for lipid level

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STATIN CONT.

- Lipid level can be checked prior to initiation of therapies to guide Framingham Risk Score and to evaluate patients compliance
- JUPITER trial found slightly higher HgbA1c level 5.9 vs 5.8 P=.001, in addition to greater risk of developing DM
- Meta-analysis of 13 statin trials 91,140 patients revealed a 9% increased risk of DM however no sex-specific analysis performed.
- Overall it is felt that benefits outweigh the risk for both sexes

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CORONARY ARTERY DISEASE CONT.

- Medications NOT recommended for primary or secondary prevention
  - Hormone therapy
  - SSRI
  - Antioxidant Vitamin supplements (Vitamin C, E and beta carotene)
  - Folic acid-with or without B6 and B12 supplements
  - Diagnostic testing should include Stress Echo more reliable than standard exercise testing
  - AA and Hispanic women awareness of risk factors decreased since 1009

Twenty Things You Didn't Know about Women and Heart Disease. J Cardiovasc Nurs. 2014; 29(5): 384–385.
doi:10.1097/JCN.0000000000000129.

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TREATMENT ACS/MICROVASCULAR DYSFUNCTION IN WOMEN

- Statins –improve endothelin dysfunction
- Angina-improved with beta blockers, calcium channel blockers, nitrates.
- Ranolazine not found to be effective
- Antidepressants may be effective in pain perception
- ASA for known CAD and has been discussed prior
- Exercise
- Modifiable risk factor modification

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PRE TEST PROBABILITY OF CAD

Table 2. Pretest Probability for Coronary Artery Disease by Age, Sex, and Symptoms*

Age, y	Sex	Typical/Definite Angina Pectoris	Atypical/Probable Angina Pectoris	Nonanginal Chest Pain	Asymptomatic
30–39	Men	Intermediate	Intermediate	Low	Very low
	Women	Intermediate	Very low	Very low	Very low
40–49	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Low	Very low	Very low
50–59	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Intermediate	Low	Very low
60–69	Men	High	Intermediate	Intermediate	Low
	Women	High	Intermediate	Intermediate	Low

High indicates >90%; intermediate 10% to 90%; low <10%; very low <5%. Reused with permission from Gibbons et al.[40]
*No data exists for patients <30 or >69 y but it can be assumed that prevalence of coronary artery disease increases with age. In a few cases, patients with ages at the extremes of the decades listed may have probabilities slightly outside the high or low range.

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INVASIVE/NON INVASIVE TESTING

- Cardiac catherization as has been discussed before
- PET/MPI testing can be done to detect ischemia and or flow reserve
- Stress MRI
- CT perfusion
- Exercise treadmill –best diagnostic test for anyone with normal EKG. IT provides information regarding exercise tolerance and hemodynamic response.
- CTA

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WESTERN DIET AND INFLAMMATION

- Prospective trial 25,994 US women followed for 12years (published 2018)
- 40 Biomarkers collected-lipids, inflammatory markers
- HIGHEST REDUCTION NOTED IN MIDDLE AND UPPER GROUPS-MED INTAKE ASSOCIATED WITH REDUCTION OF INFLAMMATORY BIOMARKERS-29.6% AND OVERALL 25% REDUCTION OF CVD
- Whole Food mostly plant based diet-incudes fish and chicken and eggs low quantity, low amount of processed foods and white breads
- Modification of overall dietary pattern key to success

Ahmad, S. et al. Assessment of Risk Factors and Biomarkers Associated With Risk of Cardiovascular Disease Among Women Consuming a Mediterranean Diet. JAMA Network Open. 2018;1(8):e185708. doi:10.1001/jamanetworkopen.2018.5708

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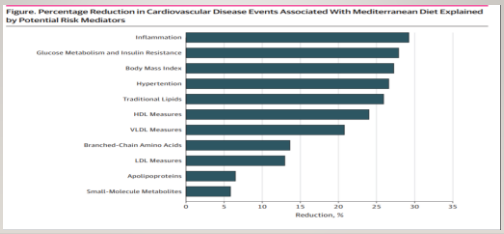
PROSPECTIVE DIET AND CVD WOMEN-12YR STUDY



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CONCLUSION

- Women as a gender are understudied in area of CVD
- CVD risk has correlation with reproductive events, there is evidence of inflammation, endothelial dysfunction leading to CVD
- Multiple traditional and non traditional risk factors contribute to CVD
- Important new correlation between Depression, diet and CVD and inflammatory markers are noted-research is ongoing
- Diet may hold the key to improving inflammation

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