

**MENOPAUSAL HORMONE THERAPY:  
HOT TOPIC**



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Gina Price Lundberg MD

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**OBJECTIVES**

- CVD in Women
- Changes at Menopause
- VMS and GU symptoms
- Studies on MHT- old and new
- Current assessment of CVD Risk in women
- Current options for MHT

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### PREVENTION OF HEART DISEASE IN WOMEN – MENOPAUSE IS TIME FOR CVD RISK ASSESSMENT

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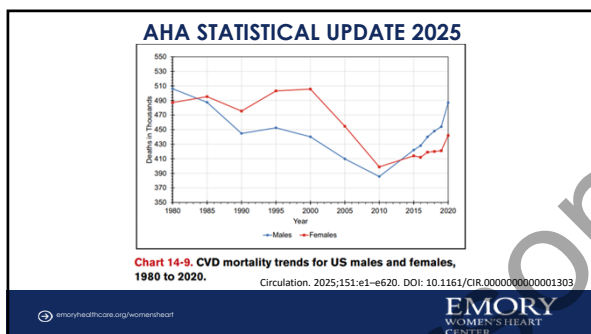
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### WOMEN'S HEART ALLIANCE

RESEARCH SHOWS THAT MOST WOMEN AREN'T AWARE OF THE UNIQUE SIGNS OF HEART DISEASE

cardiologists say:

Symptom	Percentage
STOMACH PAIN	91%
INDIGESTION	85%
FATIGUE	84%

are the most ignored symptoms.

Based on a survey of 88 female cardiologists conducted 10/20–10/21

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### WHA REPORT/ SURVEY 2025

- Only 1 in 4 women treated by cardiologists know that heart disease is their #1 killer.
- 67% of cardiologists say they're treating more young women than they were five years ago.
- 84% of female cardiologists report treating women who were misdiagnosed by other providers in the past year.



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### CVD IN WOMEN

- Women have a higher prevalence of angina
- Women have a lower burden of obstructive CAD
- Women have a poorer prognosis compared to men
- Clinical presentation- chest pain most common but also weakness, dyspnea, nausea, and neck, jaw and back pain



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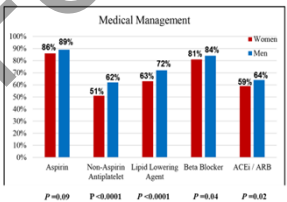
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### Treatment Disparities: Young Women vs. Men with AMI

Young women were less likely to receive evidence-based AMI medications



Medication Category	Women (%)	Men (%)	P-value
Aspirin	88%	89%	P=0.89
Non-Aspirin Antiplatelet	51%	82%	P<0.0001
Lipid Lowering Agent	63%	72%	P<0.0001
Beta Blocker	81%	84%	P=0.84
ACEI / ARB	59%	64%	P=0.02



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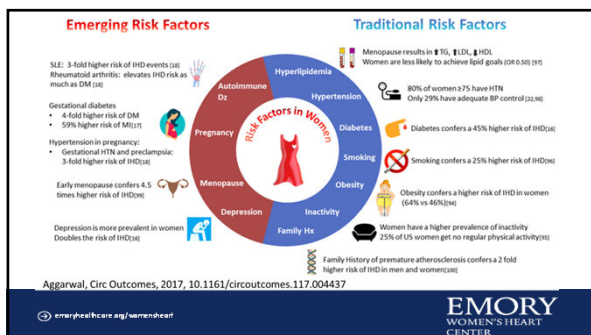
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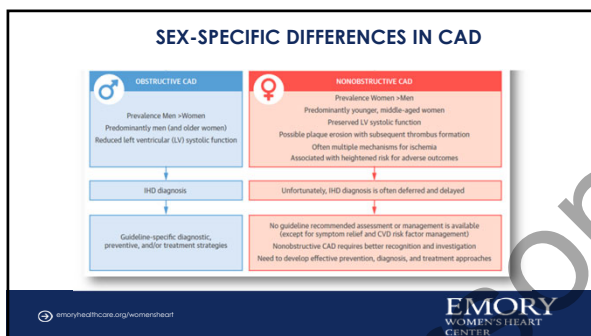
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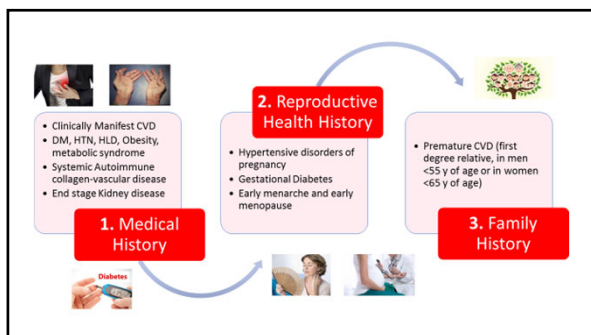
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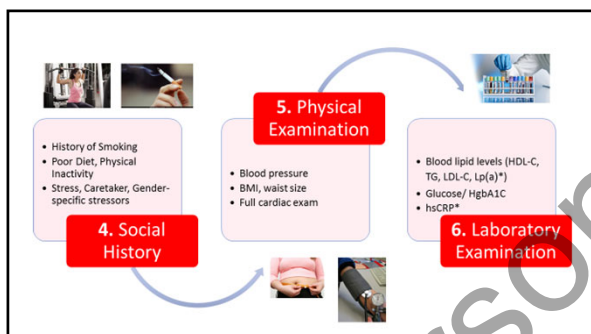
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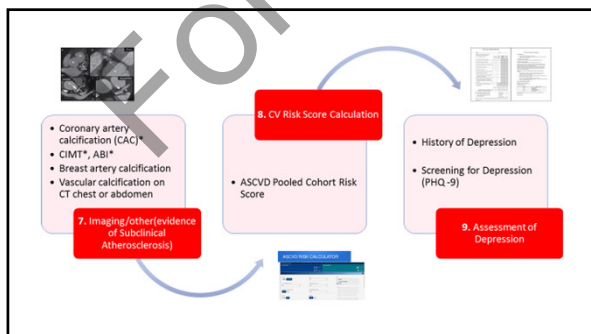
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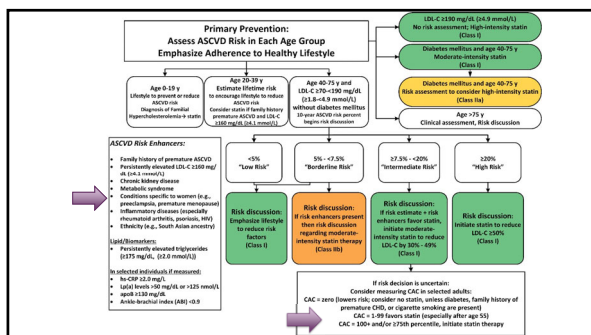
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### ROLE OF CAC

- Risk Stratification with CAC scoring helps identify subclinical atherosclerosis, especially in women who may not have traditional cardiovascular risk factors.
- It can reclassify risk in women with intermediate risk based on standard assessments like the ASCVD risk score.
- Studies suggest that a CAC score of 0 is reassuring, while higher scores correlate with increased risk of cardiovascular events.

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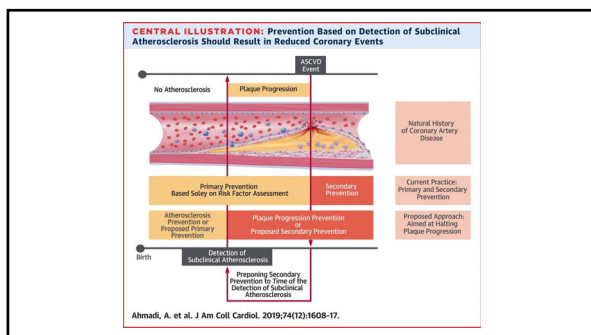
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### EVIDENCE FROM STUDIES

- The MESA (Multi-Ethnic Study of Atherosclerosis) and other studies suggest that CAC scoring improves risk prediction beyond traditional risk factors.
- In postmenopausal women, high CAC scores correlate with future cardiovascular events and can help guide preventive interventions.

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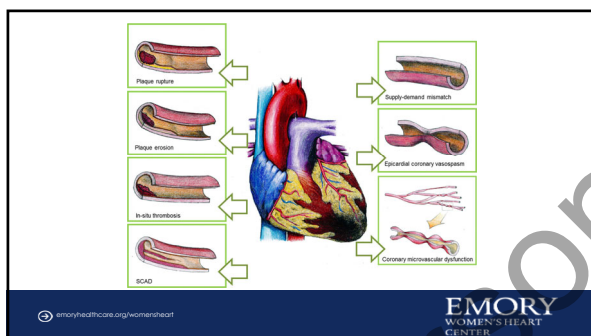
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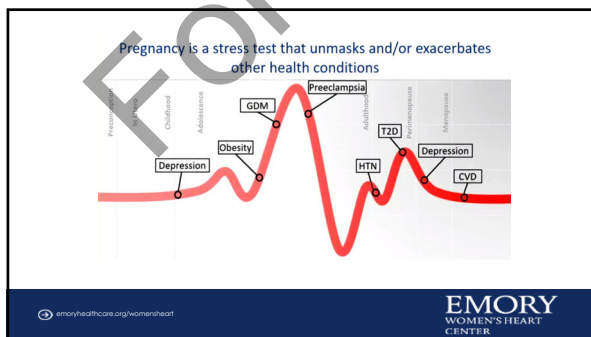
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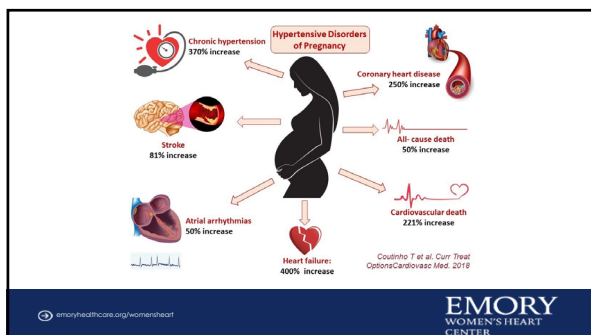
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### MENOPAUSE

- Menopause is a normal, natural event, defined as the final menstrual period (FMP), confirmed after 1 year of no menstrual bleeding
- Represents the permanent cessation of menses resulting from loss of ovarian follicular function, usually due to aging
- About 6K women per day enter menopause

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### WHAT IS MENOPAUSE?

	Menarche			FMP (FS)		
	5	14	36	51	51.5	52
REPRODUCTIVE	REPRODUCTIVE			MENOPAUSAL TRANSITION		
	Early	Peak	Late	Early	Perimenopause	Late
Duration	variable			variable	1-3 years (FS)	2-5 years (FS)
MENOPausal CRITERIA	Menstrual Cycle			Menstrual Cycle		
	Menstrual cycle to regular	Regular	Irregular	Variable length of cycle	Irregular	Interval of 60-90 days
SUPPORTIVE CRITERIA	Endocrine	Low	Normal	Low	Low	Normal
	Androgen	Low	Low	Low	Low	Normal
	Androgen	Low	Low	Low	Low	Normal
	Androgen	Low	Low	Low	Low	Normal
DESCRIPTIVE CHARACTERISTICS	Symptoms			Symptoms		
	Increasing symptoms			Increasing symptoms		

Harlow SD Menopause 2012;19:387-95

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### EXCEPTIONS TO RECOMMENDATIONS

- **Premature menopause** is defined as menopause occurring before 40 years of age
- **Early menopause** is defined as menopause occurring before 45 years of age.
- Premature or early menopause may be spontaneous or induced by surgery (bilateral oophorectomy with or without hysterectomy), chemotherapy, or radiation therapy.
- Compared with women who experience menopause at the average age, VMS in women with premature or early menopause are often more severe.
- Furthermore, observational data have indicated that untreated premature menopause regardless of the cause is associated with an elevated risk of CHD, parkinsonism, cognitive decline, dementia, osteoporosis, and mortality.
- **Systemic ERT** should be initiated unless clear contraindications are present and continued at least until the average age of menopause, which is currently 52 years.

Cho, Circulation 2023

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### MENOPAUSE SYMPTOMS

**Classic symptoms:**

- Change in menstrual cycle pattern (during perimenopause)
- Vasomotor symptoms (hot flashes & night sweats)
- Vulvovaginal symptoms, dyspareunia
- Sleep disturbances

**Other symptoms sometimes associated with menopause:**

- Cognitive concerns (memory, concentration, brain fog)
- Psychological symptoms (depression, anxiety, moodiness, aggression)

**There is no one universal menopausal syndrome**

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### Menopausal Hormone Therapy Timeline

Experimental Studies

- ↑ HDL - vasodilation of blood vessels
- ↓ LDL - insulin resistance - lipid peroxidation - intravascular collagen - VSMC proliferation

American Heart Association. Mariana Garcia et al. Circ Res. 2016;118:1273-1293 Copyright © American Heart Association, Inc. All rights reserved.

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### Timing Hypothesis

- Timing Hypothesis: The beneficial effects of MHT in preventing atherosclerosis occur only when the therapy is initiated EARLY before advanced atherosclerosis develops.
- Predicts that MHT is NOT beneficial when given to older women, because the underlying biologic characteristics of the vessel wall and vascular response to MRT are altered in older, more atherosclerotic vessels.

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Cuyang et al. J Am Coll Cardiol. 2006 May 2;47(9):1741-53

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### Timeline for Menopause Hormone Therapy Trials

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### MULTI MEDICAL SOCIETY POSITIONS ON MHT 2023

Aspect of treatment	American College of Obstetrics and Gynecology <sup>1</sup>	North American Menopause Society <sup>2</sup>	American Association of Clinical Endocrinology and American College of Endocrinology <sup>3</sup>	Endocrine Society <sup>4</sup>
Principal indication	Menopausal symptoms	Menopausal symptoms	Menopausal symptoms	Menopausal symptoms
Prevention of coronary heart disease	Not recommended	Not recommended	Not recommended	Not recommended
Social considerations	None	Consideration of age and time from menopause onset	Consideration of age, time from menopause onset, and history of cardiovascular disease, with lipid profile, smoking history	Consideration of age, time from menopause onset, and baseline risk of cardiovascular disease and breast cancer
Dose and mode of administration	Lowest effective dose	Appropriate dose to manage symptoms with consideration of route	Lowest effective dose	Shared decision-making to determine formulation, dose, and route
Duration of use	Shortest period based on risk-benefit analysis, with recommendation against routine discontinuation in patients <65 y of age	May be extended for persistent vasomotor symptoms, prevention of bone loss, or quality of life after attempt at nonhormonal measures benefits and risks regularly	Recommended for <65 y with reduction of dose if continuing	Shortest total duration consistent with the treatment goals and ongoing risk assessment of the individual woman

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### ACOG POSITION

- ACOG emphasizes tailoring MHT to each woman's specific needs, considering factors such as symptom severity, health risks, and personal preferences. ACOG.ORG<sup>4</sup>.
- Duration and Monitoring: The lowest effective dose of MHT should be used for the shortest duration necessary to manage symptoms. Regular evaluations are recommended to assess the ongoing need for therapy. ACOG.ORG

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### ENDOCRINOLOGY POSITION

- Efficacy: HRT has been shown to be effective in preventing bone loss and reducing the risk of fractures in postmenopausal women. It is particularly beneficial when initiated around the time of menopause. ENDOCRINE.ORG
- Recommendations: The Endocrine Society suggests that HRT can be considered for the prevention of osteoporosis in postmenopausal women at elevated risk of fractures. The decision to use HRT should be individualized, taking into account the patient's risk profile and preferences. ENDOCRINE.ORG

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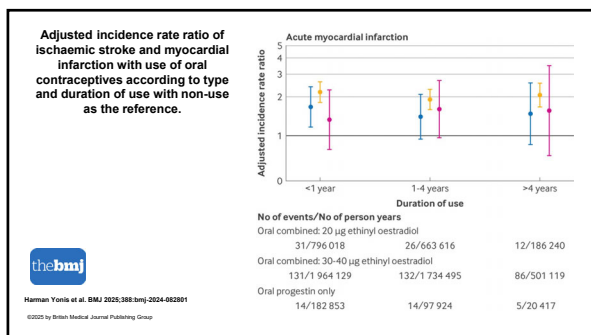
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**PRINCIPLE FINDINGS:**

- In this nationwide, prospective cohort study, current use of contemporary hormonal contraception, including combined oral contraceptive pills, vaginal ring, patch, progestin-only pills, and subcutaneous implant, was associated with an increased risk of ischemic stroke and myocardial infarction compared with no use.
- The absolute risks remained low.
- Use of the levonorgestrel-releasing intrauterine device was found not to be associated with increased arterial thrombotic risk.
- The highest risk estimates were observed with estrogen-containing products; duration of use did not seem to influence the risk of an arterial thrombotic event

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**CURRENT THERAPIES FOR MHT**

- Different formulations (estrogen-only vs. combination therapy)
- Non-hormonal alternatives for symptom relief
- Individualized approach based on risk profile and share decision making
- Watch for elevated blood pressure and elevated triglycerides with all oral MHT

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**CVD RISK AND NON CARDIAC RISKS**

- Recent studies have explored the efficacy and safety of low-dose hormone therapies, including transdermal patches, in younger postmenopausal women.
- Cardiovascular Safety: Observational studies indicate that low-dose transdermal MRT is not associated with an increased risk of thrombotic events.

PMC.NCBI.NLM.NIH.GOV

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**High Risk/ Avoid MHT**  
Known ASCVD (CAD/ PAD)  
Known venous thrombosis or pulmonary embolism  
Known Stroke/TIA or MI  
Known Clotting Disorder  
Known Breast Cancer  
ASCVD Risk > 7.5%

**Definite Risk/ Caution with MHT**  
Known Diabetes  
Smoking  
Uncontrolled HTN  
Obesity/ Sedentary/ Limited mobility  
SLE/ RA/ Migraine with aura  
High TG or uncontrolled cholesterol  
ASCVD Risk > 5.0-7.4%

**Low Risk/ Acceptable for MHT**  
Recent menopause, normal weight, normal blood pressure, active female  
ASCVD Risk < 5%

**High Risk/ Avoid MHT**  
Oral combination MHT for more than 10 years or after age 65  
Unopposed estrogen in women with an intact uterus

**Definite Risk/ Caution with MHT**  
Oral combination MHT for more than 5 years or after age 65

**Low Risk/ Acceptable for MHT**  
MHT at early onset of Menopause for less than 5 years duration  
Low dose transdermal E2 patch  
Vaginal creams, estradiol rings, tablets, & inserts

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**CONCLUSIONS**

- These new findings suggest that initiating low-dose transdermal MHT early in the postmenopausal period may offer symptom relief with a favorable safety profile.
- However, individual risk factors should be carefully evaluated when considering MHT options.

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**WHO IS AT RISK FOR CVD EVENT?**

- 1- Adverse Outcomes of Pregnancy (AOP)  
(Eclampsia/ Preeclampsia, Gestational Diabetes, Hypertensive Disorder of Pregnancy, Placental Abruption, Preterm Delivery, Small for Gestational Age, Multiple miscarriages) 
- 2- Hypertension 
- 3- Diabetes 
- 4- PCOS with central obesity, abnormal lipids, HTN 
- 5- High cholesterol, LDL-C>190 mg/dL, TG>300 mg/dL 
- 6- Menopause Hormone Therapy with CVD risks factors 
- 7- Obesity with CVD risk factors 
- 8- Migraine Headache with CVD risk factors 
- 9- Autoimmune disorders, Lupus, Rheumatoid Arthritis 

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**RECOMMENDATIONS FOR PREVENTION OF HEART DISEASE IN ALL WOMEN**

- HTN control
- DM control
- Lipid control
- Smoking Cessation
- Obesity- BMI<25 ideal
- Lifestyle- Diet and Physical activity



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**Q&A**

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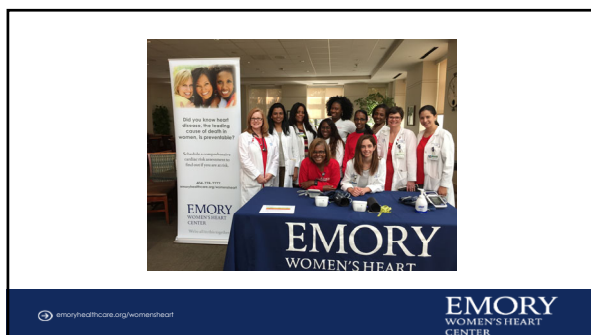
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