AMA
AMERICAN MEDICAL ASSOCIATION

Joint SPS/WPS Education Program

‘The Connection Between Menopause, Cardiovascular Disease and Health Disparities’

Friday, November 8 | 2 – 3 pm CT

Moderator

Elisa Choi, MD
Chair, AMA Women Physicians Section

Sponsored by:

AMA's Senior Physicians Section (SPS) & Women Physicians Section (WPS)

Learning Objectives

Upon Completion of this activity, learners will be able to:

Pietragallo (Ob-Gyn)

- Recognize the protective role of estrogen against atherosclerotic cardiovascular disease.
- Recognize that future menopause research is needed among historically marginalized populations.

Volgman (Cardiologist)

- Discuss the risk of heart disease in menopause and the long-range effects of vascular disease.
- Recognize the relationship between menopause and cardiovascular disease, and how health disparities increase the risk of cardiovascular disease for patients experiencing menopause.

Speaker

Helana C. Pietragallo, MD, NCMP

Obstetrics & Gynecology
Allegheny Health, Pittsburgh, PA

It is important to recognize the protective role of estrogen against atherosclerotic cardiovascular disease.

Cardiovascular Disease (CVD) is the number 1 cause of death for women in US

- 1 death every 80 seconds
- 1/3.2 deaths in women annually

Coronary Heart Disease (CHD) is very rare in premenopausal women

Postmenopausal women have more cardiovascular events than premenopausal age-matched women.

Complications of CVD in premenopausal women much lower than aged matched men and the opposite is true for postmenopausal women than they have greater complication related to CVD than age-matched men

CVD in women lags behind men by approx 10 years, MI and sudden death lags by 20 years. This delay is thought to be due to protective effects of estrogen.

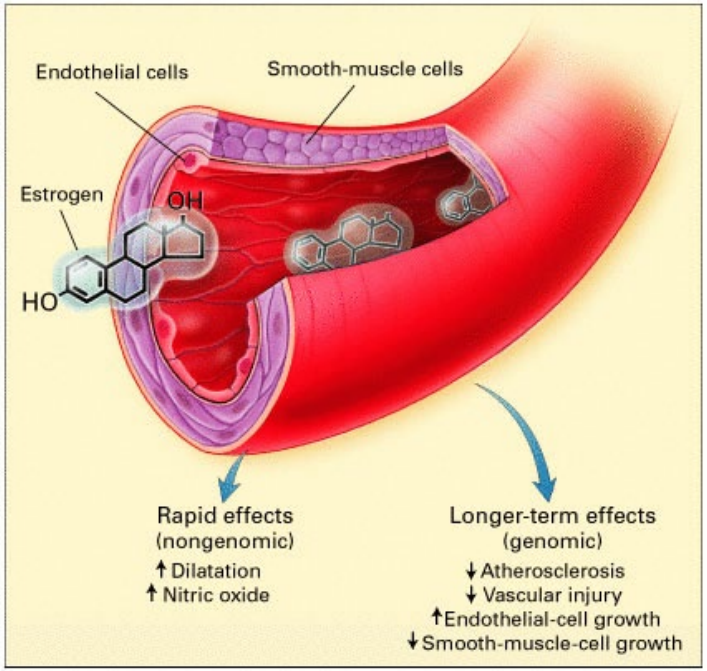
Mikkola TS, Clarkson TB. Estrogen replacement therapy, atherosclerosis, and vascular function. Cardiovasc Res. 2002 Feb 15;53(3):605-19. doi: 10.1016/s0008-6363(01)00466-7. PMID: 11861031.

How does estrogen act on blood vessels?

Estrogen

- Cardioprotective role of Estrogen
  - Estrogen receptors on:
    - Vascular endothelial cells
    - Cardiomyocytes
    - ER-α, ER-β, G protein-coupled ER
  - Nitric Oxide pathway upregulated
  - Decreases reactive oxygen species
  - Stimulates neoangiogenesis

Menopause → decreased arterial compliance → HTN & CVD



Srivaratharajah, Kajenny MD, MSc, FRCPC; Abramson, Beth L. MD, MSc, FRCPC, FACC Hypertension in menopausal women: the effect and role of estrogen, Menopause: April 2019 - Volume 26 - Issue 4 - p 428-430 doi: 10.1097/GME.0000000000001304

What happens when estrogen protection goes away?

What is due to estrogen and what is due to other midlife factors?

Menopause transition confers estrogen independent risk to CV health	• Change in lipids • Increase in BP • Increase central & visceral adiposity

Estrogen plays a significant role	• In early menopause (<45 y/o)
	  • Increase in CVD
	  • Increase in CVD related death
	  • Increase in all-cause mortality

Christ JP, Gunning MN, Palla G, Eijkemans MJC, Lambalk CB, Laven JSE, Fauser BCJM. Estrogen deprivation and cardiovascular disease risk in primary ovarian insufficiency. Fertil Steril. 2018 Apr;109(4):594-600.e1. doi: 10.1016/j.fertnstert.2017.11.035. Epub 2018 Mar 28. PMID: 29605405. Bertone-Johnson, Elizabeth R. ScD; Manson, JoAnn E. MD, DrPH, NCMP Early menopause and subsequent cardiovascular disease, Menopause: January 2015 - Volume 22 - Issue 1 - p 1-3 doi: 10.1097/GME.0000000000000385 Srivaratharajah, Kajenny MD, MSc, FRCPC; Abramson, Beth L. MD, MSc, FRCPC, FACC Hypertension in menopausal women: the effect and role of estrogen, Menopause: April 2019 - Volume 26 - Issue 4 - p 428-430 doi: 10.1097/GME.0000000000001304 Committee Opinion No. 698: Hormone Therapy in Primary Ovarian Insufficiency. Obstet Gynecol. 2017 May;129(5):e134-e141. doi: 10.1097/AOG.0000000000002044. PMID: 28426619

EARLY MENOPAUSE (10% of females)

Primary Ovarian Insufficiency (POI)

Surgical Menopause

Latrogenic Menopause

Cardiovascular Disease: Primary Ovarian Insufficiency (POI)

POI increases

- Ischemic heart disease
- Heart failure – 36% higher risk than menopause at average age

Each 1-year increase in age at menopause

- 2-4% decreased risk of heart failure
- 2% decrease in CVD mortality

Christ JP, Gunning MN, Palla G, Eijkemans MJC, Lambalk CB, Laven JSE, Fauser BCJM. Estrogen deprivation and cardiovascular disease risk in primary ovarian insufficiency. Fertil Steril. 2018 Apr;109(4):594-600.e1. doi: 10.1016/j.fertnstert.2017.11.035. Epub 2018 Mar 28. PMID: 29605405.
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Increase risk of Cardiovascular Disease

Nurses' Health Study

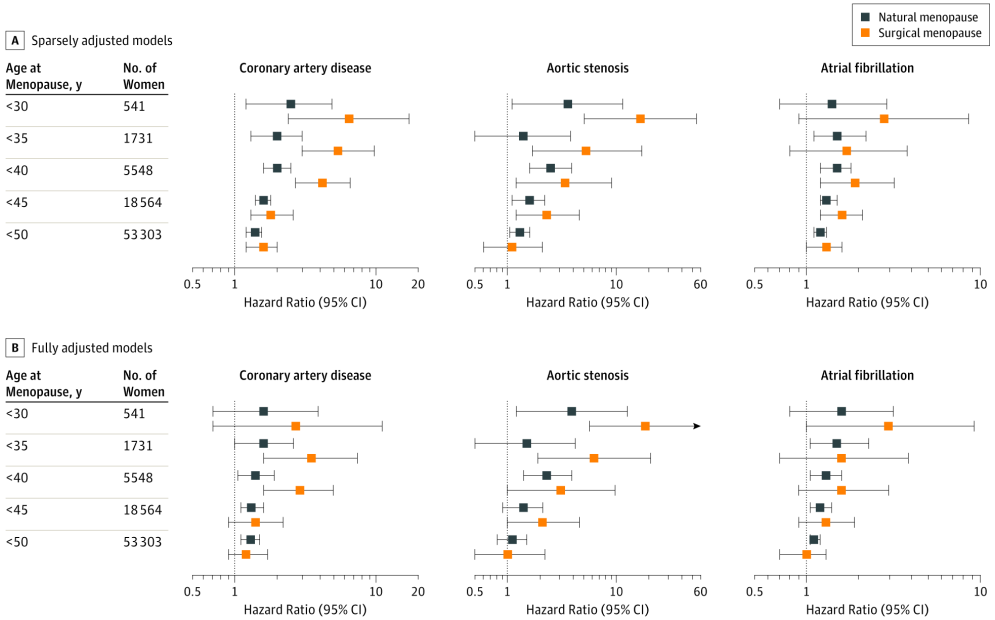
- Surgical menopause <50 y/o yielded increased CVD mortality

WHI Observational Study:

- No association between surgical menopause and cardiovascular events
- 80% of patients were >40 y/o
- >60% were on Estrogen therapy

Cardiovascular Disease – POI & Surgical POI

- Cohort study 144,260 (UK Biobank) with natural POI, surgical POI, and usual menopause
- Incidence of CAD, ischemic stroke, or peripheral artery disease:
  - 1.5 % - menopause
  - 2.5 % - natural POI
  - 3.7 % - surgical menopause



Honigberg MC, Zekavat SM, Aragam K, Finneran P, Klarin D, Bhatt DL, Januzzi JL Jr, Scott NS, Natarajan P. Association of Premature Natural and Surgical Menopause With Incident Cardiovascular Disease. JAMA. 2019 Dec 24;322(24):2411-2421. doi: 10.1001/jama.2019.19191. PMID: 31738818; PMCID: PMC7231649.

Does Menopause Hormone Therapy Impact Atheroslerosis & CVD?

Timing hypothesis:

Effects of Menopause Hormone Therapy (MHT) on atherosclerosis and CV events depend on when the MHT is initiated in relation to time from menopause (with menopause being the FMP).

- Supported by RCTs (atherosclerosis imaging and clinical events) and observational data
- MHT exerts benefits to healthy endothelium
- MHT exerts risk to endothelium with established plaques

Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928.

- **Estrogen in the Prevention of Atherosclerosis Trial (EPAT)**
  - Double blinded placebo-controlled trial
  - Carotid artery wall thickness
  - Showed estrogen related to reduced atherosclerosis

- **Women's Estrogen-Progestin Lipid-Lowering Hormone Atherosclerosis Regression Trial (WELL-HART)**
  - Double blinded placebo-controlled trial
  - Quantitative coronary angiography
  - No estrogen effect on atherosclerosis progression

Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928.

- **Dutch Osteoporosis Prevention Study (DOPS)**
  - Avg age 50
  - 7 months after FMP on average
  - BMI 25.2
  - CVD reduced by 52% after 10 years of HT use, and 39% decrease after 16 years of use.
  - All-cause mortality reduced by 43% at 10 years and 34% at 16 years of use

- **Early versus Late Intervention Trial with Estradiol (ELITE)**
  - RCT that looked at initiation of MHT timing
  - Randomized to <6 years from time of FMP (55.4 yrs) to >10 years since FMP (65.4)
  - Reduced progression of subclinical atherosclerosis in the <6 year from FMP group and the >10 year showed no reduction

Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928.

- **2 meta-analyses looking at women who initiated HT <60 y/o and/or <10 years from FMP**
  - 39% reduction in all-cause mortality
  - 32% reduction in CHD

Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928.

How Might Estrogen Therapy Reduce Atherosclerosis?

- Estrogen's impact on lipids accounts for 25-50% of its protection
- Action on vessel wall affects endothelial function and impacts vascular tone
- Estrogen therapy has anti-inflammatory effect, reducing plasma vascular adhesion molecules
  - E-selectin
  - Vascular cell adhesion molecule-1 (VCAM-1)
  - Intercellular adhesion molecule-1 (ICAM-1)
- Reduction of vascular adhesion molecules reduces the attachment of WBCs to the vessel wall.
- Anti-inflammatory impact of estrogen thought to stabilize plaques but not inhibit plaque erosion

Mikkola TS, Clarkson TB. Estrogen replacement therapy, atherosclerosis, and vascular function. Cardiovasc Res. 2002 Feb 15;53(3):605-19. doi: 10.1016/s0008-6363(01)00466-7. PMID: 11861031.

What is the role of HT in Primary CVD prevention?

- Social media in menopause care
- Primary prevention is not an indication for hormone therapy
- No major society endorses hormone therapy for the prevention of CVD
- Area for future research

We need to recognize that future menopause research is needed among historically marginalized populations.

POI Prevalence by Ethnicity

- Symptoms vary by ethnicity:
  - Black: more intense VMS and for longer duration
  - Hispanic: more Genitourinary Syndrome of Menopause
  - Black and Hispanic: more depression and sleep disturbance

Premature menopause	Caucasian	Black	Hispanic	Chinese	Japanese	Total
% in ethnic group	1.0	1.4	1.4	0.5	0.14	1.1

Luborsky JL, Meyer P, Sowers MF, Gold EB, Santoro N. Premature menopause in a multi-ethnic population study of the menopause transition. Hum Reprod. 2003 Jan;18(1):199-206. doi: 10.1093/humrep/deg005. PMID: 12525467.

Race/ethnicity: Midlife Experience

- Study of Women Across the Nation (SWAN)
  - 3302 women 42-52, up to 16 follow-up visits over 25 years (74% at final visit)
  - 935 Black women
  - 1550 White women
  - 250 Chinese women
  - 281 Japanese women
  - 286 Hispanic women
- Age at FMP: Black women had Menopause 8.5 months earlier (52.1 y/o) than White women (52.8 y/o)
- Sleep: Black women had worse sleep efficiency, took longer to fall asleep, and spent more time awake after sleep onset than White women.
- Vasomotor symptoms: Black women had earlier onset, more frequent, more bothersome, VMS compared with White women. VMS lasted for 3.5 more years for Black women than White women

VMS and CVD

- Study of Women Across the Nation (SWAN) Heart looked at VMS and cardiovascular health:
  - 600 women without clinical CVD
  - Coronary and aortic calcification
  - Endothelial function
  - Carotid Intima Media Thickness (IMT)

- Women with VMS:
  - poorer endothelial function
  - higher IMT (most pronounced in early onset VMS)
  - greater Aortic calcification

VMS and CVD

- Women's Ischemia Syndrome Evaluation (National Heart Lung and Blood Institute):
  - VMS early (before 42) had elevated CVD mortality
  - Poor endothelial function

- Healthy Woman Study : the longer patients reported VMS the higher their risk of aortic calcification

Thurston RC. Vasomotor symptoms: natural history, physiology, and links with cardiovascular health. Climacteric. 2018 Apr;21(2):96-100. doi: 10.1080/13697137.2018.1430131. Epub 2018 Feb 2. PMID: 29390899; PMCID: PMC5902802.

VMS and CVD

- MsHeart Study: 300 women 40-60, non-smokers, with and without daily VMS, without clinical CVD, not using HT or non-hormonal treatments for VMS or cardiovascular medications
- 3 days of subjective VMS reporting using digital diary, 3 days of wrist actigraphy measuring sleep, 24 hour ambulatory ECG, 24 hour physiologic VMS monitoring, Blood draws, IMT, Carotid plaque US, Brachial artery endothelial
- Results:
  - Patients with VMS (diary or physiologic) had higher IMT and more carotid plaque
  - Frequency of VMS was tightly associated with variance in IMT more than any other CVD risk factor aside from race/ethnicity
  - Bottomline: VMS were related to higher IMT and carotid plaque

Thurston RC. Vasomotor symptoms: natural history, physiology, and links with cardiovascular health. Climacteric. 2018 Apr;21(2):96-100. doi: 10.1080/13697137.2018.1430131. Epub 2018 Feb 2. PMID: 29390899; PMCID: PMC5902802.

Race/ethnicity: Midlife care & treatment

- Black and Hispanic women lowest rates of MHT
- Black and Chinese women who used MHT reported reduced quality of life compared with no treatment

SOME (not all) of the studies that we need

- Studies aimed at early intervention to reduce HTN, LDL, smoking, waist circumference in Black women who enter midlife with a more adverse CVD risk
- Studies on the impact of structural racism on midlife health
  - Accessing care
  - Prescribing patterns
  - Cultural preference
  - Why there is a difference in race/ethnicity in response to treatments
- Studies that include all historically marginalized groups
- Studies that look at menopause hormone therapy as primary prevention in appropriate patients

Resources:

- Mikkola TS, Clarkson TB. Estrogen replacement therapy, atherosclerosis, and vascular function. Cardiovasc Res. 2002 Feb 15;53(3):605-19. doi: 10.1016/s0008-6363(01)00466-7. PMID: 11861031.
- Thurston RC. Vasomotor symptoms: natural history, physiology, and links with cardiovascular health. Climacteric. 2018 Apr;21(2):96-100. doi: 10.1080/13697137.2018.1430131. Epub 2018 Feb 2. PMID: 29390899; PMCID: PMC5902802.
- Harlow SD, Burnett-Bowie SM, Greendale GA, Avis NE, Reeves AN, Richards TR, Lewis TT. Disparities in Reproductive Aging and Midlife Health between Black and White women: The Study of Women's Health Across the Nation (SWAN). Womens Midlife Health. 2022 Feb 8;8(1):3. doi: 10.1186/s40695-022-00073-y. Erratum in: Womens Midlife Health. 2022 Oct 21;8(1):10. doi: 10.1186/s40695-022-00082-x. PMID: 35130984; PMCID: PMC8822825.
- Hodis HN, Mack WJ. Menopausal Hormone Replacement Therapy and Reduction of All-Cause Mortality and Cardiovascular Disease: It Is About Time and Timing. Cancer J. 2022 May-Jun 01;28(3):208-223. doi: 10.1097/PPO.0000000000000591. PMID: 35594469; PMCID: PMC9178928.
- Avis NE, Crawford SL, Greendale G, Bromberger JT, Everson-Rose SA, Gold EB, Hess R, Joffe H, Kravitz HM, Tepper PG, Thurston RC; Study of Women's Health Across the Nation. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med. 2015 Apr;175(4):531-9. doi: 10.1001/jamainternmed.2014.8063. PMID: 25686030; PMCID: PMC4433164.
- Lee E, Anselmo M, Tahsin CT, Vanden Noven M, Stokes W, Carter JR, Keller-Ross ML. Vasomotor symptoms of menopause, autonomic dysfunction, and cardiovascular disease. Am J Physiol Heart Circ Physiol. 2022 Dec 1;323(6):H1270-H1280. doi: 10.1152/ajpheart.00477.2022. Epub 2022 Nov 11. PMID: 36367692; PMCID: PMC9744645.
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- Kochersberger A, Coakley A, Millheiser L, Morris JR, Manneh C, Jackson A, Garrison JL, Hariton E. The association of race, ethnicity, and socioeconomic status on the severity of menopause symptoms: a study of 68,864 women. Menopause. 2024 Jun 1;31(6):476-483. doi: 10.1097/GME.0000000000002349. Epub 2024 Apr 23. PMID: 38652870.
- El Khoudary SR, Greendale G, Crawford SL, Avis NE, Brooks MM, Thurston RC, Karvonen-Gutierrez C, Waetjen LE, Matthews K. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). Menopause. 2019 Oct;26(10):1213-1227. doi: 10.1097/GME.0000000000001424. PMID: 31568098; PMCID: PMC6784846.

Speaker

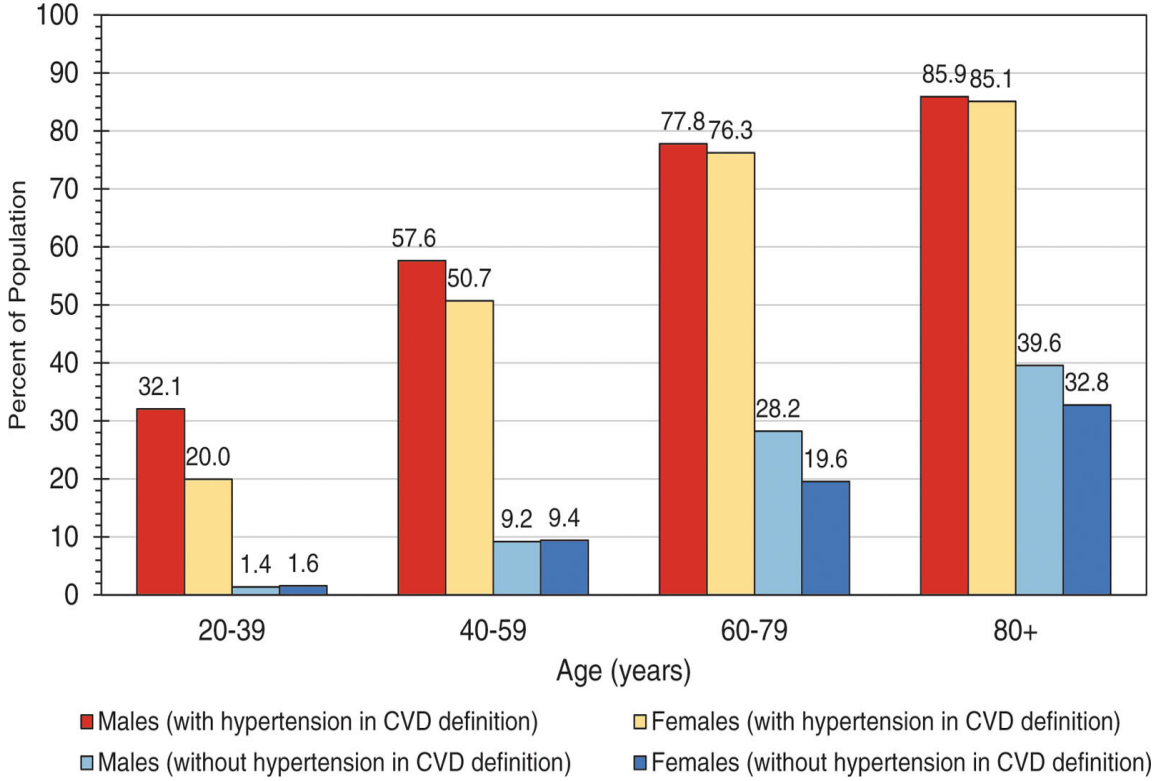
Annabelle S. Volgman, MD, FACC

Director, Rush Heart Center for Women, Chicago, IL

Session Objective

- This session will examine the connection between menopause, CVD, and health disparities.
- Understanding this connection is essential for improving health outcomes among women, particularly the significant racial and ethnic disparities that currently exist.

Prevalence of CVD in US Adults



CVD includes CHD, HF, stroke, and with and without hypertension.

Seth S. Martin. Circulation. 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association, Volume: 149, Issue: 8, Pages: e347-e913, DOI: (10.1161/CIR.0000000000001209)

Women Have Been Misled About Menopause

Hot flashes, sleeplessness, pain during sex:

- For some of menopause's worst symptoms, there's an established treatment.
- Why aren't more women offered it?

NY Times Magazine By Susan Dominus Published Feb. 1, 2023 Updated June 15, 2023

By Christine Gorman and Alice Park Monday, July 22, 2002

Reported by David Bjerklie, Alice Park and Sora Song, April 28. 2003

5 Things to Know About Menopause and Hormone Therapy

1. Hormone therapy eases several menopausal symptoms and has some additional health benefits.
2. Hormone therapy carries health risks that vary by age.
3. Fears of hormone therapy are mostly rooted in an important but imperfect study from 2002.
4. Menopause is understudied and undertaught.
5. Hormone therapy is not the only option.

NY Times Magazine By Susan Dominus Published Feb. 1, 2023 Updated June 15, 2023

Circulation

AHA SCIENTIFIC STATEMENT

Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention

A Scientific Statement From the American Heart Association

ABSTRACT: Cardiovascular disease (CVD) is the leading cause of death in women, who have a notable increase in the risk for this disease after menopause and typically develop coronary heart disease several years later than men. This observation led to the hypothesis that the menopause transition (MT) contributes to the increase in coronary heart disease risk. Over the past 20 years, longitudinal studies of women traversing menopause have contributed significantly to our understanding of the relationship between the MT and CVD risk. By following women over this period, researchers have been able to disentangle chronological and ovarian aging with respect to CVD risk. These studies have documented distinct patterns of sex hormone changes, as well as adverse alterations in body composition, lipids and lipoproteins, and measures of vascular health over the MT, which can increase a woman's risk of developing CVD postmenopausally. The reported findings underline the significance of the MT as a time of accelerating CVD risk, thereby emphasizing the importance of monitoring women's health during midlife, a critical window for implementing early intervention strategies to reduce CVD risk. Notably, the 2011 American Heart Association guidelines for CVD prevention in women (the latest sex-specific guidelines to date) did not include information now available about the contribution of the MT to increased CVD in women. Therefore, there is a crucial need to discuss the contemporary literature on menopause and CVD risk with the intent of increasing awareness of the significant adverse cardiometabolic health–related changes accompanying midlife and the MT. This scientific statement provides an up-to-date synthesis of the existing data on the MT and how it relates to CVD.

Samar R. El Khoudary, PhD, MPH, FAHA, Chair
Brooke Aggarwal, EdD, MS, FAHA
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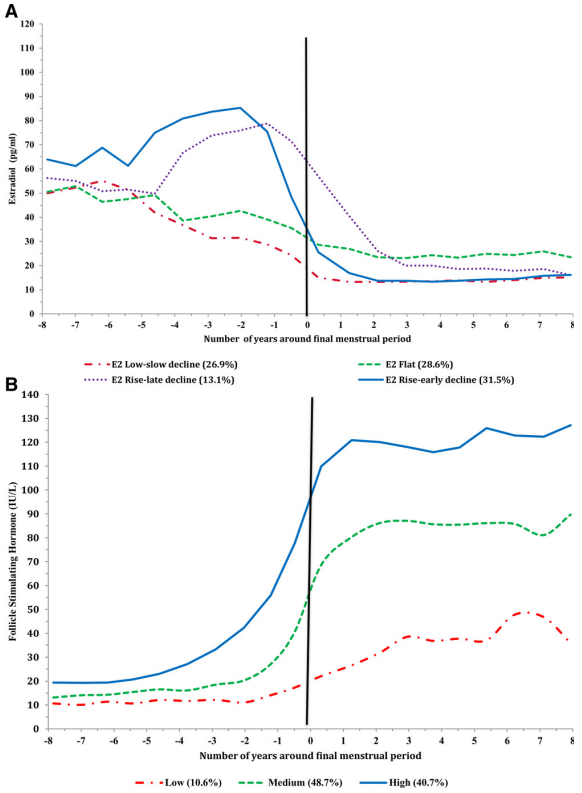
Marian C. Limacher, MD, FAHA
JoAnn E. Manson, MD, DrPH, FAHA
Marcia L. Stefanick, PhD, FAHA
Matthew A. Allison, MD, MPH, FAHA, Vice Chair
On behalf of the American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention; and Council on Cardiovascular and Stroke Nursing

El Khoudary, ...Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912



Trajectories of estradiol (E2; A) and follicle-stimulating hormone (B) over the menopausal transition.

Summary

1. The median age of natural menopause is 50 years. Natural menopause is considered premature if it occurs before 40 years of age and early if it occurs between 40 and 45 years of age.
2. Because of the trends for increases in overall life expectancy in the US, a significant proportion of women will spend up to 40% of their lives postmenopausal.
3. Markers of greater CVD risk:
    - Earlier age at natural menopause and linked to being Black or Hispanic
    - Having a short menstrual cycle length
    - Having a low parity

El Khoudary, …Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

Summary

4. Iatrogenically induced menopause (i.e., BSO) during the premenopausal period is associated with higher CVD risk.

- Hysterectomy, regardless of ovarian status, does not influence CVD risk factors before or after menopause.
- Guidelines from the North American Menopause Society endorse MHT use among women with premature or early natural or surgical menopause, with treatment until at least the median age of menopause (in the absence of contraindications).

5. Vasomotor symptoms are associated with worse CVD risk factor levels and measures of subclinical atherosclerosis. These associations may depend on the timing of these symptoms during the MT.

6. Sleep disturbance, a common complaint during the MT, is linked to a greater risk of subclinical CVD and worse cardiovascular health indexes in midlife women.

El Khoudary, ...Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

Summary

7. Depression occurs more frequently during the perimenopausal and postmenopausal years and is related to both vasomotor symptoms and incident CVD.

8. The perimenopause stage extends 12 months after menopause and has been identified as a stage of vulnerability accompanied by significant alterations in several cardiometabolic and vascular health parameters strongly linked to higher CVD risk.

9. Central/visceral fat increases and lean muscle mass decreases are more pronounced during perimenopause.

- The increased central adiposity is associated with an increased risk of mortality, even among those with normal BMI.

El Khoudary, …Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

Summary

10. Pericardial fat volumes are higher after menopause, independently of age, and could be influenced by estradiol levels or MHT use.

11. Increases in lipids (LDL-C and apolipoprotein B), metabolic syndrome risk, and vascular remodeling at midlife are driven during perimenopause more than aging, whereas increases in blood pressure, insulin, and glucose are likely more influenced by chronological aging.

12. Novel data show a reversal in the associations of HDL-C with CVD risk during perimenopause, suggesting that higher HDL-C levels may not consistently reflect good cardiovascular health in midlife women.

El Khoudary, ...Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

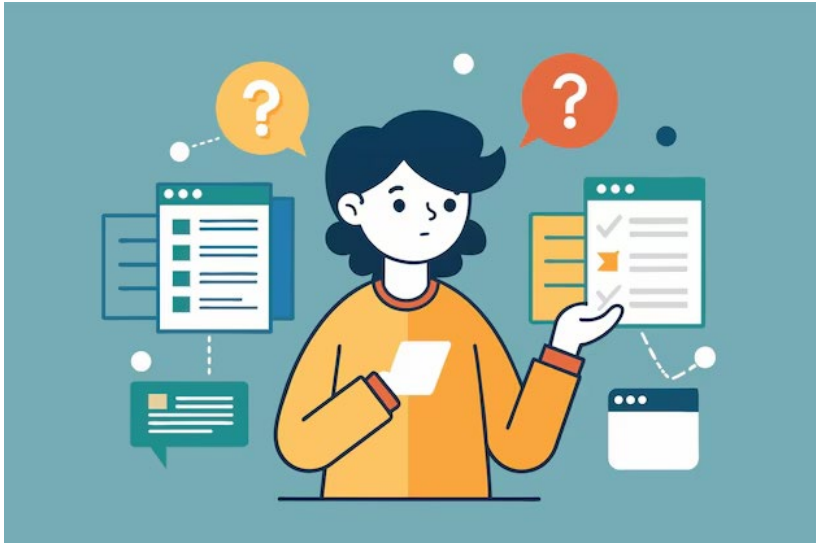
Summary

13. The literature supporting a critical role for the time of initiation of MHT use relative to menopause, with initiation at <60 years of age or within 10 years of menopause appearing to be associated with reduced CVD risk, strongly calls for further research assessing MHT use, including potential contrasts by form, route, and duration of administration, on cardiometabolic effects in women traversing menopause, a large proportion of whom experience menopausal symptoms before even reaching menopause.

14. Data for primary and secondary prevention of atherosclerotic CVD and improved survival with lipid-lowering interventions remain elusive for women, with further study required for evidence-based recommendations to be developed specifically for women.

El Khoudary, …Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

Lipid-lowering Therapies



- Although evidence-based data supporting a statistically significant reduction of CVD events and all-cause mortality in primary prevention in women are lacking for statins and other lipid-lowering therapies, the current guidelines for the prevention of CVD do not provide specific recommendations for women and men independently.
- Therefore, the most recent lipid-lowering guidelines recommend statins as first-line therapy for CVD risk reduction, regardless of sex or menopausal status.

El Khoudary, ...Allison, M. A., On behalf of the American Heart Association Prevention Science Committee of the Council on, E., Prevention, Council on, C., & Stroke, N. (2020). Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association. *Circulation*, *142*(25), e506-e532. https://doi.org/10.1161/CIR.0000000000000912

Statins are associated with a large reduction in all-cause mortality in women from a cardiac outpatient population

Sophie H Bots ,[1] N Charlotte Onland-Moret,[2] Milena Jancev,[1] Monika Hollander,[2] Igor I Tulevski,[3] Leonard Hofstra,[3,4] G Aernoud Somsen,[3] Hester M den Ruijter[1]

Table 3 Adjusted HRs with 95% CIs for the risk of all-cause and cardiovascular mortality associated with statin use stratified by sex

	Whole population (n=17 262)	Women (n=8981)	Men (n=8281)
All-cause mortality (n_{event}=1035)			
No statin (ref)	1	1	1
Statin	0.76 (0.71 to 0.82)	0.66 (0.58 to 0.74)	0.89 (0.81 to 0.96)
Cardiovascular mortality (n_{event}=270)			
No statin (ref)	1	1	1
Statin	0.72 (0.61 to 0.83)	0.55 (0.39 to 0.71)	0.93 (0.77 to 1.08)

Key questions

What is already known about this subject?

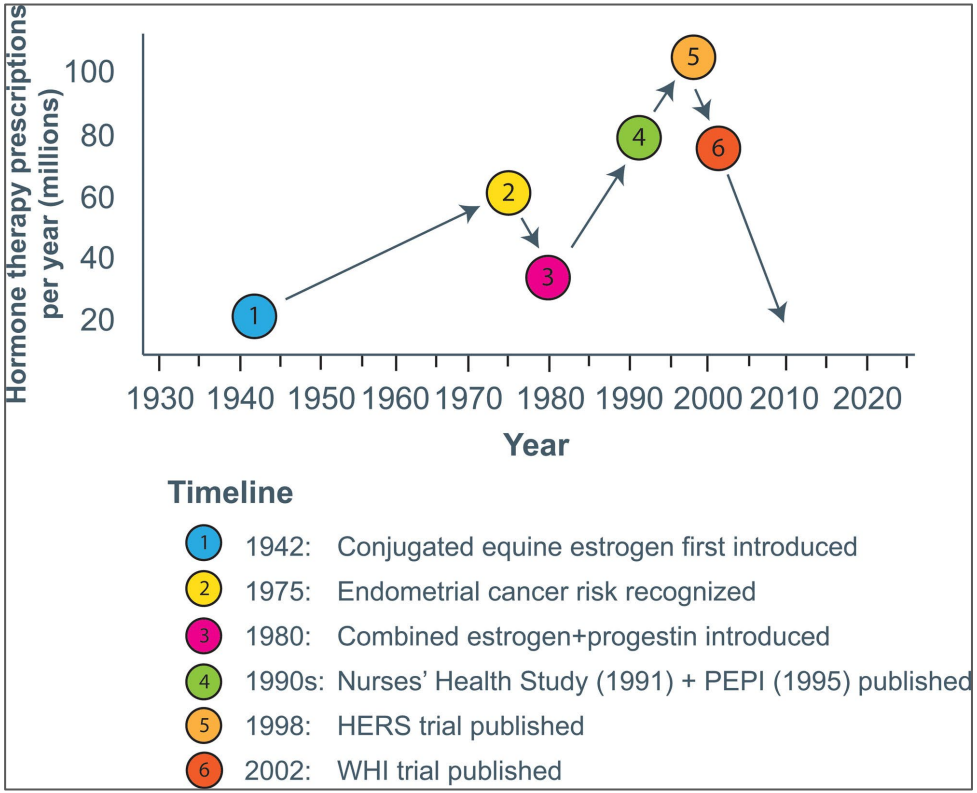
- Women more often receive low-intensity statin therapy than men despite evidence that statin therapy lowers cardiovascular disease risk in a dose-dependent manner.
- It remains unclear whether statin treatment is equally effective in women and men due to under-representation of women in primary prevention trials and scarcity of sex-stratified data.
- This study evaluates the sex-specific relation between statin treatment and survival, and explores whether high-intensity statins confer additional benefit.

Bots, S. H., …den Ruijter, H. M. (2022). Statins are associated with a large reduction in all-cause mortality in women from a cardiac outpatient population. *Open Heart*, *9*(1), e001900. https://doi.org/10.1136/openhrt-2021-001900

Non-statin Lipid-Lowering Therapies

- Diets
- Ezetimibe
- PCSK-9 inhibitors
- Inclisiran
- Bempedoic Acid

Timeline of hormone therapy use in the US



HERS indicates Heart and Estrogen/progestin Replacement Study; PEPI, Postmenopausal Estrogen/Progestins Interventions; and WHI, Women's Health Initiative

Cho, L., Kaunitz, A. M., Faubion, S. S., Hayes, S. N., Lau, E. S., Pristera, N., Scott, N., Shifren, J. L., Shufelt, C. L., Stuenkel, C. A., & Lindley, K. J. (2023). Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long? *Circulation*, *147*(7), 597-610. https://doi.org/10.1161/circulationaha.122.061559

Menopausal Hormone Therapy Use Among Postmenopausal Women

- Question
  - What were the prevalence and trends in menopa… use among po… re–
- Findings
  - Women of racial and ethnic minority groups had lower prevalence of MHT use compared to non-Hispanic White women.
- CONCLUSIONS AND RELEVANCE Results of this cross-sectional study show that over the past 2 decades, MHT use declined among US postmenopausal women of all age and racial and ethnic groups.

Women of racial and ethnic minority groups had a lower prevalence of MHT use compared to non-Hispanic White women.

Yang, L., & Toriola, A. T. (2024). Menopausal Hormone Therapy Use Among Postmenopausal Women. *JAMA Health Forum*, *5*(9), e243128. https://doi.org/10.1001/jamahealthforum.2024.3128

Racial Disparities in MHT Use

Non-Hispanic Black women had the lowest prevalence of MHT use in both 1999 to 2000 and 2017 to 2020 and exhibited the greatest relative decline (PR, 0.04; 95%CI, 0.02-1.00).

- Black and Hispanic or Latina women consistently report more severe and disruptive vasomotor symptoms in comparison to non-Hispanic White women.

Socioeconomic factors also considerably influenced hormone therapy use.

- Higher family income and insurance coverage were associated with increased MHT use.
- Educational attainment was positively associated with MHT use among non-Hispanic Black and Hispanic women but not among non-Hispanic White women.

- Iyer, T. K., & Manson, J. E. (2024). Recent Trends in Menopausal Hormone Therapy Use in the US: Insights, Disparities, and Implications for Practice. JAMA Health Forum, 5(9), e243135. https://doi.org/10.1001/jamahealthforum.2024.3135

Addressing sociodemographic, socioeconomic, and gendered disparities for equity in menopause care

Although effective treatments are available, their access and utilization across diverse groups are considerably unequal. Addressing these issues requires a multifaceted approach.

- Policies at local, national, and global levels can shape better outcomes by addressing structural barriers and fostering interventions that enhance women's knowledge, train providers, and improve access to treatment for those who want it.
- Financial disparities in access to care can also be addressed.
- By leveraging a patient-centered, culturally sensitive approach and considering the modifiable social factors, the medical community can foster more equitable menopause care.
- This may improve health outcomes and enhance quality of life. It is essential to understand how sociodemographic, socioeconomic, and sociocultural factors affect the symptoms of menopause as well as the safety and efficacy of its treatments.

Future research can address how interventions can best meet the diverse needs of the populations they are intended to serve.

An equitable approach to menopause care requires a concerted effort from healthcare providers, researchers, policymakers, and- society at large to ensure that every individual can receive support and care.

Peate, M., Johnson, T. L., Avis, N. E., & Hickey, M. (2024). Addressing sociodemographic, socioeconomic, and gendered disparities for equity in menopause care. *Cell Rep Med*, *5*(6), 101616. https://doi.org/10.1016/j.xcrm.2024.101616

Menopause and racial/ethnic disparities

- Whether racial and ethnic minorities are at higher risk for early menopause remains a matter of inquiry.
- One study showed that there are racial/ethnic differences in the prevalence of premature ovarian failure.
- One report of black women entering menopause approximately 2 years earlier than whites.
- Obesity also has an impact on reproductive hormones in the perimenopause and increases the likelihood of vasomotor symptoms.
- There may be environmental exposures and risk factors common to discrete populations of women that impact pubertal timing, infertility, and menopause.

Butts, S. F., & Seifer, D. B. (2010). Racial and ethnic differences in reproductive potential across the life cycle. *Fertil Steril*, *93*(3), 681-690. https://doi.org/10.1016/j.fertnstert.2009.10.047

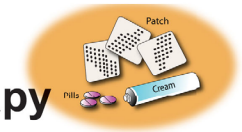
Menopause and Cardiovascular Disease

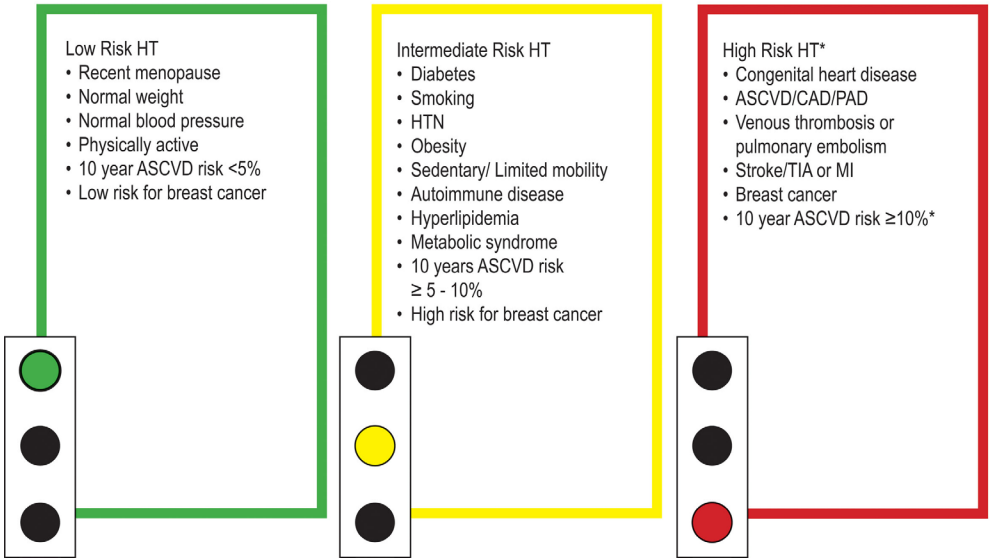
- Sex-specific risk factors for incident HF include disorders of pregnancy (eclampsia/preeclampsia, gestational diabetes), PPCM, polycystic ovarian syndrome, and premature menopause, although the exact contribution of these conditions to the incidence of HF among women is unknown.
- In a systematic review and meta-analysis of 78 studies including >10 million participants, any HDP, including gestational hypertension, preeclampsia, or eclampsia, was associated with a greater risk of ischemic stroke; **late menopause (55 years of age)** and gestational hypertension were associated with a greater risk of hemorrhagic stroke; and oophorectomy, HDP, PTB, and stillbirth were associated with a greater risk of any stroke.

Martin, S. S., . . . Palaniappan, L. P. (2024). 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. *Circulation*, *149*(8), e347-e913. https://doi.org/10.1161/cir.0000000000001209

Menopausal hormone therapy recommendation by patient risk

Menopausal Hormone Therapy



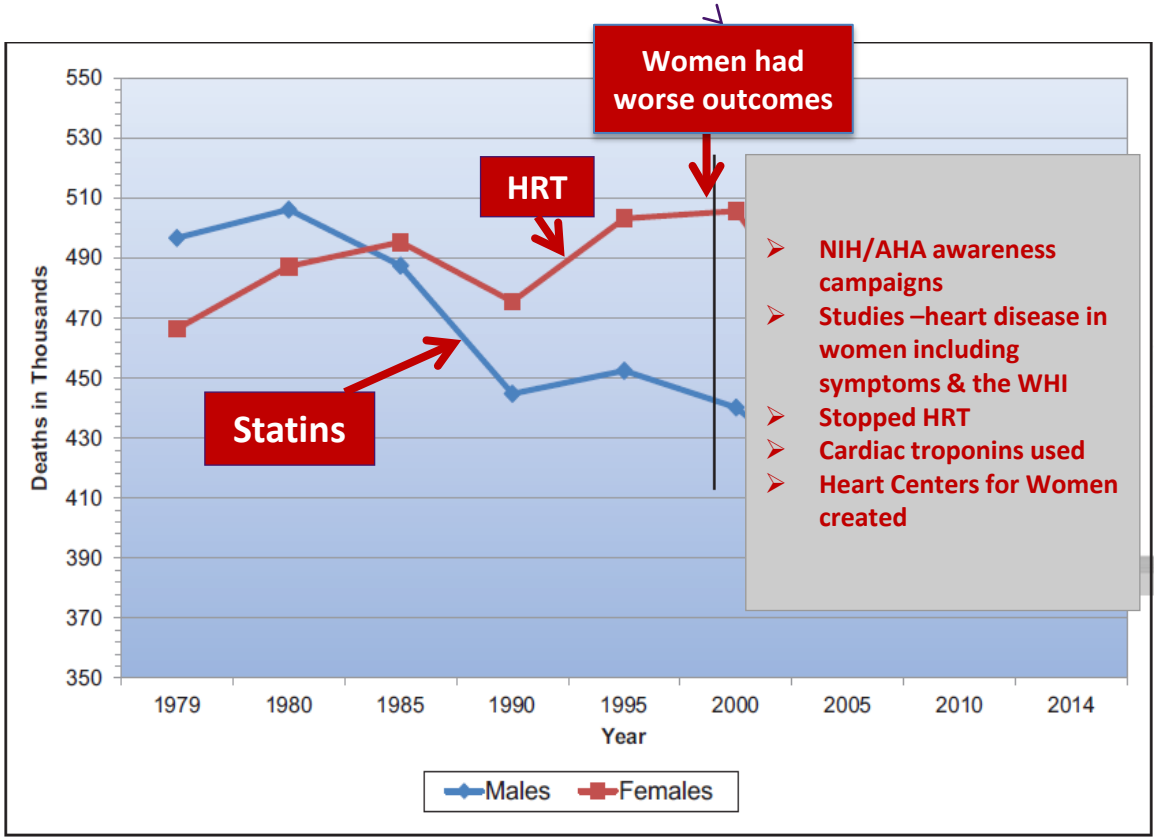


*In general, it is advised to avoid systemic hormone therapy. Consider alternative therapy, and if severe vasomotor symptoms persist, individualized, shared decision-making is recommended. All women are candidates for low-dose vaginal estrogen therapy for genitourinary symptoms of menopause.

ASCVD indicates atherosclerotic cardiovascular disease; CAD, coronary artery disease; HTN, hypertension; MI, myocardial infarction; PAD, peripheral artery disease; and TIA, transient ischemic attack.

Cho, L., Kaunitz, A. M., Faubion, S. S., Hayes, S. N., Lau, E. S., Pristera, N., Scott, N., Shifren, J. L., Shufelt, C. L., Stuenkel, C. A., & Lindley, K. J. (2023). Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long? *Circulation*, *147*(7), 597-610. https://doi.org/10.1161/circulationaha.122.061559

CVD mortality rates for women and men



Circulation. 2017;135:00–00. DOI: 10.1161/CIR.0000000000000485

CVD mortality rates for women and men

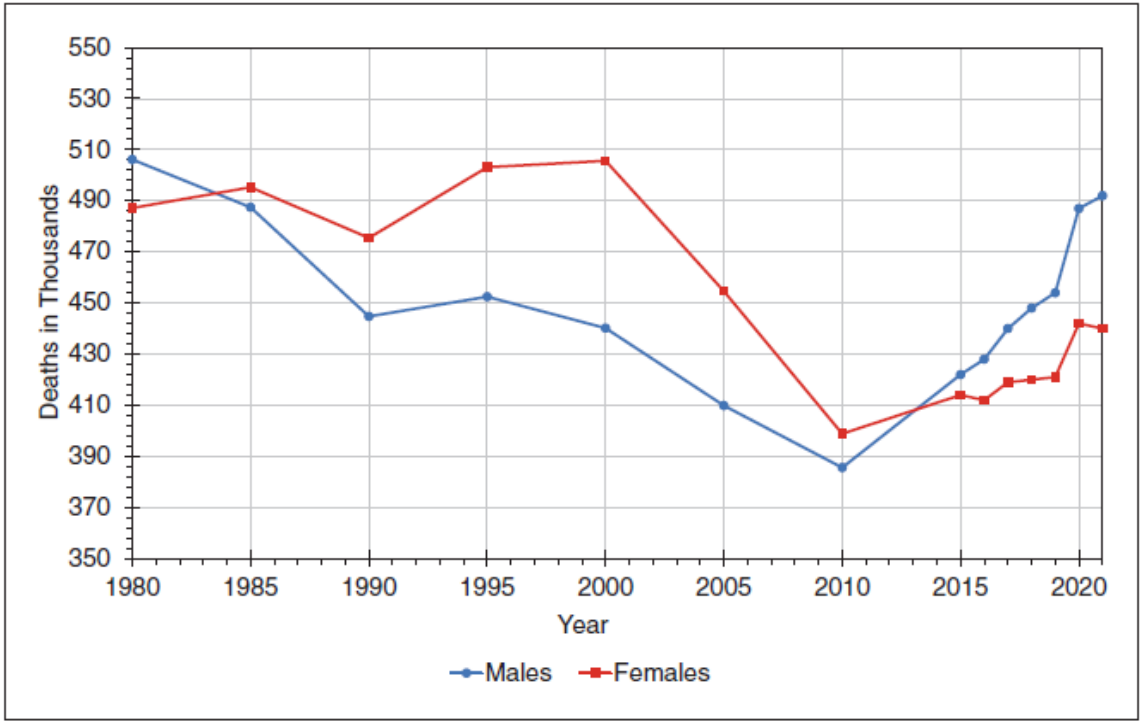


Chart 14-9. CVD mortality trends for US males and females, 1980 to 2021.

Martin, S. S., . . . Palaniappan, L. P. (2024). 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. *Circulation*. https://doi.org/10.1161/cir.0000000000001209

Facilitator

Virginia (Ginny) E. Hall, MD
Delegate, AMA Senior Physicians Section

A special thank you to our speakers!

Questions from Audience Members

2024 AMA INTERIM MEETING

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