Baptist Health
HEART INSTITUTE

Hormone Replacement & Women's Heart Disease

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Disclosures: None

Learning Objectives

- Understand the physiologic effects of estrogen on the cardiovascular system
- Summarize evidence on hormone replacement therapy (HRT) and heart disease
- Apply current guideline-based recommendations to primary care practice

Cardiovascular Disease in Women

- Leading cause of death in women in the United States
  - Often under-recognized and under-treated
  - Sex-specific differences in presentation, risk factors, and outcomes exist
  - Menopause represents a key inflection point in cardiovascular risk
    - Average age ~51

Menopause and Cardiovascular Risk

- Loss of endogenous estrogen associated with increased ASCVD risk
  - Adverse changes in lipid profile, insulin resistance, and body fat distribution
  - Increase in blood pressure and vascular stiffness
  - Acceleration of subclinical atherosclerosis due to above changes

Estrogen and the Cardiovascular System

- Improves endothelial function and nitric oxide availability
  - Favorable effects on lipid metabolism (↑ HDL, ↓ LDL)
  - Anti-inflammatory and antioxidant properties
  - Direct effects on vascular smooth muscle and myocardium

Types of Hormone Therapy

- Estrogen-only therapy (women without a uterus)
- Combined estrogen-progestin therapy (women with a uterus)
  - Routes: oral, transdermal, vaginal
  - Doses and formulations vary in regards to cardiovascular impact

Early Observational Studies

- Suggested cardioprotective effects of hormone therapy
  - Reduced rates of coronary heart disease in HRT users
  - Limitations: healthy user bias and confounding findings prompted large randomized controlled trials

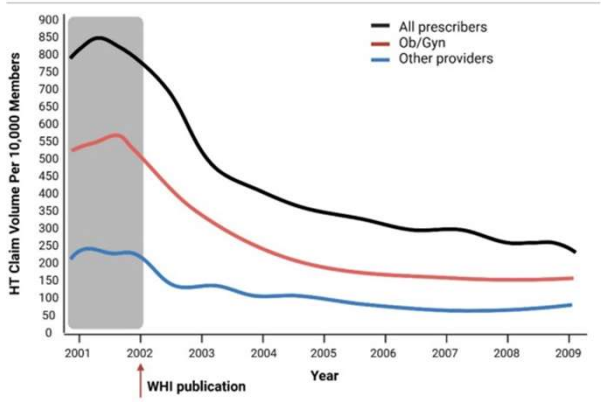
Women's Health Initiative (WHI)

- Large randomized controlled trial initiated in the 1990s
  - Studied estrogen-progestin and estrogen-only therapy
  - Mean age at enrollment: 63 years
  - Changed clinical practice and perception of HRT

WHI Cardiovascular Findings

- Increased risk of coronary heart disease events early after initiation
  - Increased risk of coronary events (29%), stroke (41%), and venous thromboembolism (2-fold increase)
  - Conclusion was that hormonal therapy should not be used for primary or secondary prevention of cardiovascular disease
  - Risk varied by age and time since menopause

WHI Impact on HRT



Allyson I. Schwab, et. al
From discovery to debate: The history of menopausal hormone therapy and its impact on cardiovascular health, Autonomic Neuroscience,Volume 261,2025,103335,ISSN 1566-0702

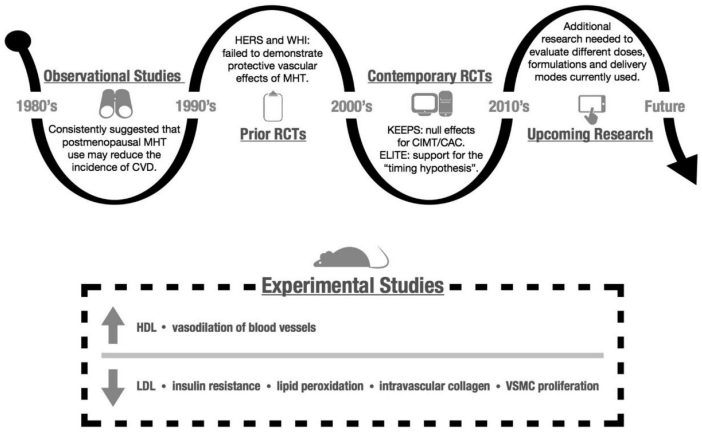
WHI Controversy

- Mean age of 63 in the trial vs. average age of menopause which is 51
  - Prior observational data suggested CV benefit in women closer to menopausal transition
- High enrollment of smokers and those with obesity
  - Earlier trials did not enroll obese women and current smokers
- Hormone Type & Formulation (Estrogen only vs. Estrogen + Progesterone)
  - Women between 50-79, no increase in CVD for estrogen only
  - Women between (50-59), 40% reduction in CVD and lower coronary artery calcification for estrogen only

More Studies

- Meta-analysis (consisting of 23 trials) 4 years after WHI examined impacts of HRT on CVD in younger and older postmenopausal women
  - 32% reduction in CVD in younger postmenopausal women vs. No treatment
  - 1st year of HRT had increased risk of ASCVD events in older postmenopausal women during the 1st year with reduction in events after 2 years
  - After adjusting for age, cardiovascular risk factors, and socioeconomic status, use of HRT was associated with a 40% reduction in CHD events and all-cause mortality

More Studies



Garcia M, et al. Cardiovascular Disease in Women: Clinical Perspectives. Circ Res. 2016 Apr 15;118(8):1273-93.

The Timing Hypothesis

- Cardiovascular effects of HRT depend on timing of initiation
  - Younger women (<60 years) or within 10 years of menopause may have neutral or favorable risk
  - Later initiation associated with increased atherosclerotic plaque instability
  - Supported by subgroup analyses and mechanistic studies

Route of Administration Matters

- Oral estrogen increases hepatic production of clotting factors
  - Transdermal estrogen does not have the hepatic "first-pass" and is associated with lower VTE and stroke risk
  - Lower impact on triglycerides and CRP with transdermal route
  - Important consideration in women with cardiovascular risk factors

HRT and Secondary Prevention

- Not recommended for secondary prevention of ASCVD
  - No role in women with established coronary artery disease
  - Potential for harm in older women or those with advanced atherosclerosis
  - Focus should remain on guideline-directed medical therapy

Current Guideline Recommendations

- HRT not indicated for primary or secondary prevention of CVD
- HRT approved for four indications:
  - moderate to severe vasomotor symptoms
  - prevention of osteoporosis
  - treatment of hypoestrogenism
  - treatment of moderate to severe vulvovaginal symptoms
- Use lowest effective dose for shortest duration
- Individualized risk assessment is essential

Risk Stratification in Primary Care

- Assess traditional ASCVD risk factors
  - Consider pregnancy-related risk enhancers (e.g., preeclampsia, gestational diabetes)
  - Evaluate age, time since menopause, and baseline cardiovascular risk
  - Shared decision-making with patient

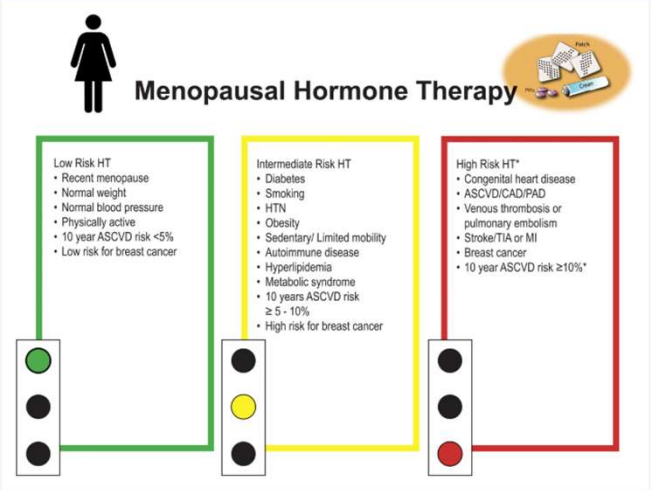
Clinical Algorithm: Is HRT Appropriate?

- Menopausal symptoms present? → NO → Avoid HRT
- YES → Assess age <60 yrs AND <10 yrs since menopause
- Assess ASCVD risk, VTE history, stroke, and breast cancer history

Cardiovascular Risk Stratification Before HRT

- Calculate 10-year ASCVD risk
- Identify risk enhancers (preeclampsia, GDM, premature menopause)
- Evaluate BP, lipids, glucose, BMI, smoking
- Low risk → Eligible for consideration| Consider HRT at lowest dose and shortest duration
- High risk → May consider avoiding systemic HRT and consider Cardiology input

Cardiovascular Risk Stratification Before HRT



Algorithm: Choosing Route of Hormone Therapy

- Need systemic therapy? → YES
- History of VTE, stroke, obesity?
  YES → Consider preference for transdermal estrogen
  NO → Oral or transdermal reasonable
- Uterus present → Add progestin

Practical Counseling Points & Follow-Up After HRT Initiation

- Clarify that HRT is for symptom management, not heart protection
  - Discuss potential cardiovascular and thrombotic risks
  - Consider transdermal formulations when appropriate
  - Reassess need for therapy periodically
- Reassess symptoms and BP at 6–12 weeks
- Monitor lipids and glucose periodically
- Reevaluate cardiovascular risk annually
- Attempt taper/discontinuation when symptoms allow
- Stop HRT if CVD event or VTE occurs

Thank You