MAYO CLINIC

2022 NAMS Hormone Therapy Position Statement:

Translating Guidelines to Practice

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Disclosures

- **Relevant Financial Relationships**
- None

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Learning Objectives

- Discuss how to implement the 2022 Hormone Therapy Position Statement key messages in clinical practice
  - Counseling on risks vs benefits
    - Breast cancer
    - Cardiovascular disease
    - Weight, body composition and diabetes
    - Bone health
    - Brain and mental health
    - Compounded hormone therapy
    - Duration of use

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Disclaimer

- This presentation uses gender-specific language as reflected in the referenced publications. However, I recognize that some individuals may identify differently than the gender and pronouns used in this presentation.

- This presentation does not review the full 2022 HT position statement!

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THE 2022 HORMONE THERAPY POSITION STATEMENT OF THE NORTH AMERICAN MENOPAUSE SOCIETY ADVISORY PANEL

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LEGEND

- Key Points-directly from the position statement
- Bottom Line-my summary and editorial comments
- Levels of evidence
  - Level I: Based on good and consistent scientific evidence.
  - Level II: Based on limited or inconsistent scientific evidence.
  - Level III: Based primarily on consensus and expert opinion.

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CONCLUSIONS-KEY POINTS

- HT is the most effective treatment for vasomotor symptoms and GSM and has been shown to prevent bone loss and fracture.
- Risks of HT differ for women, depending on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is needed. Treatment should be individualized using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation.
- For women aged younger than 60 years or within 10 years of menopause onset and without contraindications, the benefit-risk ratio appears favorable for treatment of bothersome vasomotor symptoms and for the prevention of bone loss and reduction of fracture.
- For GSM symptoms not relieved with nonhormone therapies, low-dose vaginal ET or other government-approved therapies (eg, vaginal DHEA or oral ospemifene) are recommended.

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YES, BUT HOW DO WE IMPLEMENT THESE RECOMMENDATIONS IN CLINICAL PRACTICE?

- 53 yo woman come to you with bothersome vasomotor symptoms (VMS), sleep disturbance, irritability, some mild vaginal dryness.
  - LMP-18 month ago
  - PMH-none
  - FHx-none
  - Meds-none
- She is worried about breast cancer risk because she has a friend who has breast cancer who advised her not to take HT because it causes cancer.

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WHICH OF THE FOLLOWING IS TRUE REGARDING HORMONE THERAPY RISKS AND BENEFITS?

1. The risk of breast cancer with HT is 3 additional cases/1000 women per year of HT use
2. The effects of HT on heart disease risk are independent of age at initiation
3. HT increases abdominal adiposity and the risk of diabetes
4. Systemic HT is an appropriate therapy for prevention of bone loss in women < age 60 or within 10 years of menopause

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BREAST CANCER RISK-KEY POINTS

Risk of breast cancer related to HT use is low (Level I)

< 1 additional case/1,000 women per year of HT use OR

3 additional cases/1,000 women used for 5 years (CEE+MPA)

Risk similar to that of modifiable risk factors such as 2 daily alcoholic beverages, obesity, or low physical activity. (Level III)

Effect of HT on breast cancer risk may depend on the duration of use, regimen, prior exposure, and individual characteristics. (Level II)

Different HT regimens may be associated with increased breast density, which may lead to more breast imaging, biopsies and a potential delay in breast cancer diagnosis. (Level II)

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BREAST CANCER RISK-KEY POINTS

A preponderance of data ***does not*** show an additive effect of underlying breast cancer risk (age, family history of breast cancer, genetic risk of breast cancer, benign breast disease, personal breast cancer risk factors) and HT use on breast cancer incidence. (Level II)

Insufficient data are available to assess the risk of breast cancer with newer therapies such as tissue selective estrogen complexes, including bazedoxifene plus CEE. (Level II)

Observational evidence suggests that HT use does not further increase risk of breast cancer in women at high risk because of a family history of breast cancer or after bilateral salpingo-oophorectomy for BRCA 1 or 2 genetic variants. (Level II)

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BREAST CANCER RISK

Bottom Line:

- All HT is ***not*** the same.
- The risk of breast cancer associated with HT is considered rare.
- It is greater with regimens containing a progestogen (specifically medroxyprogesterone acetate) versus with regimens containing only ET (particularly CEE) which are associated with less risk.

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"Ok, but what about my heart? Another friend has a heart issue and says hormone therapy will give me a heart attack or stroke. Is that true?"

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CARDIOVASCULAR RISK-KEY POINTS

For healthy women <60 y or within 10 y of menopause onset, favorable effects of HT on coronary heart disease and all-cause mortality should be considered against potential rare increases in breast cancer, venous thromboembolism, and stroke risk. (Level I)

Effects of HT on coronary heart disease may vary depending on age and time since menopause at time of initiation. (Level I)

Initiation of HT in recently menopausal women reduced or had no effect on subclinical atherosclerosis progression and coronary artery calcification in RCTs. (Level I)

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CARDIOVASCULAR RISK-KEY POINTS

Observational data/meta-analyses show reduced risk of coronary heart disease in women who initiate HT <60 y or within 10 y of menopause. (Level II)

HT is not government approved for primary or secondary cardioprotection. (Level I)

Personal and familial risk of cardiovascular disease, stroke, venous thromboembolism, and breast cancer should be considered when initiating HT. (Level III)

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CARDIOVASCULAR RISK

Bottom Line:

- Timing matters! It is reassuring that HT does not increase the risk of heart disease and may be beneficial in women who start HT early after menopause based on intermediate markers.
- Review personal cardiovascular disease profile risk profile and tailor HT accordingly.
- Consider transdermal route of administration for those with moderate risk and potentially avoid HT in those at high risk.

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

“But it’s going to make me gain weight, right?”

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WEIGHT, BODY COMPOSITION & DIABETES-KEY POINTS

HT significantly reduces the diagnosis of new-onset type 2 DM, but it is not government approved for this indication. (Level I)

HT is not contraindicated in otherwise healthy women with preexisting type 2 DM and may be beneficial in terms of glycemic control when used for menopause symptom management. (Level II)

Although HT may help attenuate abdominal adipose accumulation and weight gain associated with the menopause transition, the effect is small. (Level II)

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WEIGHT, BODY COMPOSITION & DIABETES

Bottom line:

- HT is probably favorable for the waistline and reduces diabetes risk, but it is NOT a weight loss drug!
- HT is not contraindicated in women with diabetes who are otherwise candidates (consider a transdermal preparation).

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"What will it do for my bones? My mom has osteoporosis."

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BONE DENSITY AND FRACTURE-KEY POINTS

HT prevents bone loss and reduces fracture risk in healthy postmenopausal women, with dose-related effects on bone density. (Level I)

HT is FDA approved for prevention of bone loss, but not for treatment of osteoporosis. (Level I)

Systemic HT is an appropriate therapy to protect against bone loss in women <60 y or within 10 y of menopause onset. (Level I)

Discontinuing HT results in rapid bone loss; however, no excess in fractures was seen in the WHI after discontinuation. (Level I)

Premature menopause best to use HT or oral contraceptives to prevent bone density loss and reduce fracture risk until the average age of menopause, then reassess. (Level II)

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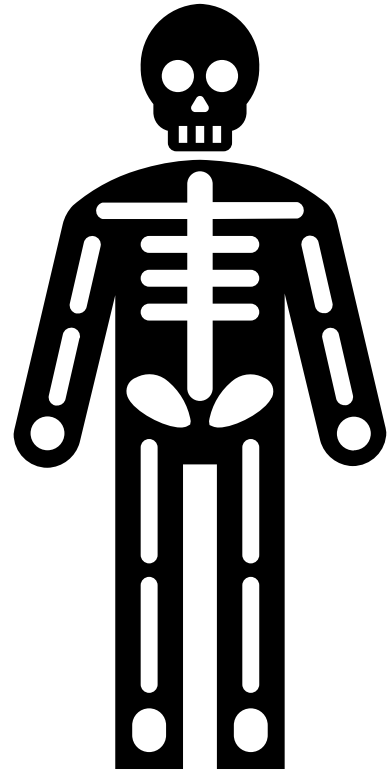
BONE DENSITY AND FRACTURE

Bottom Line:

- HT prevents bone loss and reduces fracture risk in a dose-dependent manner.
- Stopping HT will result in bone loss (so monitor as appropriate).
- HT is not a treatment for osteoporosis!
- HT is needed in women with premature menopause for bone protection (among other reasons)



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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"Will this prevent me from getting dementia? I'm worried about my memory. I sometimes forget where I put my keys…"

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DEMENTIA-KEY POINTS

In the absence of more definitive findings, HT is not recommended at any age to prevent or treat a decline in cognitive function or dementia. (Level I)

Initiating HT in women aged older than 65 years increased the risk for dementia, with an additional 23 cases per 10,000 person-years seen in women randomized to CEE plus MPA in the WHI Memory Study. (Level I)

The effect of HT may be modified by baseline cognitive function, with more favorable effects in women with normal cognitive function before hormone therapy initiation. (Level II)

ET may have cognitive benefits when initiated immediately after hysterectomy with bilateral oophorectomy, but HT in the early natural postmenopause period has neutral effects on cognitive function. (Level II)

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DEMENTIA

Bottom Line:

- HT should not be used to treat or prevent dementia.
- Timing matters-again! Using HT early after menopause onset has a neutral effect on dementia risk but starting it later can increase risk.

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"Will my mood symptoms get better on hormone therapy?"

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DEPRESSION-KEY POINTS

There is some evidence that ET has antidepressant effects of similar magnitude to that observed with antidepressant agents when administered to depressed perimenopausal women with or without concomitant vasomotor symptoms. (Level II)

ET is ineffective as a treatment for depressive disorders in postmenopausal women. Such evidence suggests a possible window of opportunity for the effective use of ET for the management of depressive disorders during the perimenopause. (Level II)

There is some evidence that ET enhances mood and improves well-being in nondepressed perimenopausal women. (Level II)

Estrogen is not government approved to treat mood disturbance. (Level I)

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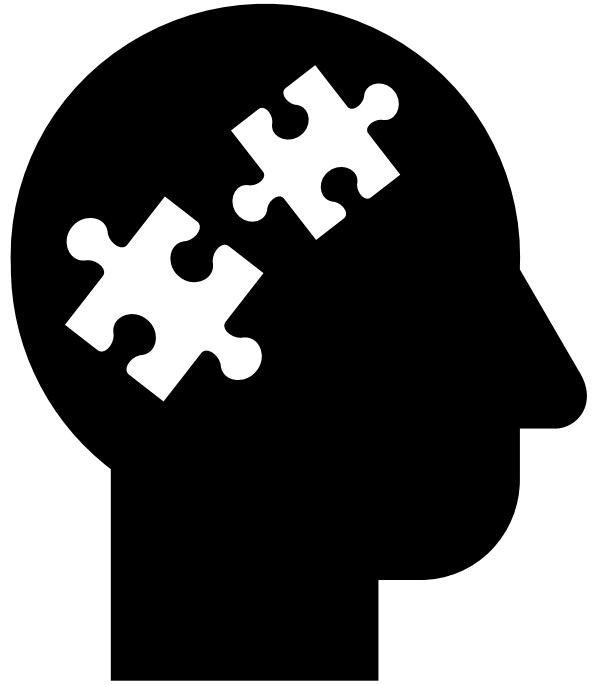
DEPRESSION

Bottom Line:

- HT may help with mood in the menopause transition but not later postmenopause and shouldn't be used to prevent mood issues.
- Watch out for rebound mood symptoms when stopping HT in women whose mood symptoms responded to HT.
- Antidepressants remain first line therapy for depression in the menopause transition.



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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

“What about my vaginal dryness?”

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GENITOURINARY SYNDROME OF MENOPAUSE (GSM)

- The signs and symptoms associated with menopause-related estrogen deficiency involving changes to the labia, vagina, urethra, and bladder and includes vaginal atrophy.
- GSM symptoms will affect at least 50% of menopausal women
  - Symptoms do not improve without treatment
  - Symptoms are chronic and progressive
- Low-dose vaginal ET preparations include creams, tablets, rings, and a softgel vaginal insert. The different preparations all contain estradiol, and one cream preparation contains conjugated estrogen. Vaginal DHEA or oral ospemifene are also available.
- Minimal systemic absorption, progestogen is not needed if only local vaginal estradiol is used
- "When HT is considered solely for GSM, local vaginal ET is generally recommended"
  - NAMS Position Statement 2022

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GENITOURINARY SYNDROME OF MENOPAUSE (GSM)

Bottom Line:

- GSM is common and undertreated.
- “Waiting it out” is not a good option.
- Low dose hormonal therapies are safe and effective.
- No progestogen is needed.
- Use low dose vaginal estrogen when GSM is the only menopause symptom.

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"One of my friends said I really should try compounded hormone therapy. She says it's natural and safer….."

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COMPOUNDED HORMONE THERAPY-KEY POINTS

Compounded bioidentical HT presents safety concerns, such as minimal government regulation and monitoring, overdosing and underdosing, presence of impurities and lack of sterility, lack of scientific efficacy and safety data, and lack of a label outlining risks. (Level I)

Salivary and urine hormone testing to determine dosing are unreliable and not recommended. Serum hormone testing is rarely needed. (Level II/III)

Shared decision-making is important, but patient preference alone should not be used to justify the use of compounded bioidentical hormone preparations, particularly when government regulated bioidentical hormone preparations are available. (Level III)

Situations in which compounded bioidentical hormones could be considered include allergies to ingredients in a government approved formulation or dosages not available in government approved products. (Level III)

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COMPOUNDED HORMONE THERAPY

Bottom Line:

- There are few reasons to use compounded HT.
- Explaining the lack of oversight as well as the availability of government regulated “bioidentical” products is often enough to convince patients to switch to an approved form.

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IMPLEMENTING RECOMMENDATIONS IN CLINICAL PRACTICE

"Ok, so if I start this, how long do I take it? Are you going to tell me I have to stop it after a certain amount of time?"

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DURATION OF THERAPY-KEY POINTS

HT does not need to be routinely discontinued in women aged older than 60 or 65 years. (Level III)

Long-term use of HT, including for women aged older than 60 years, may be considered in healthy women at low risk of cardiovascular disease and breast cancer with persistent vasomotor symptoms or at elevated risk of fracture for whom other therapies are not appropriate. (Level III)

Factors that should be considered include severity of symptoms, effectiveness of alternative nonhormone interventions, and underlying risk for osteoporosis, coronary heart disease, cerebrovascular accident, venous thromboembolism, and breast cancer. (Level III)

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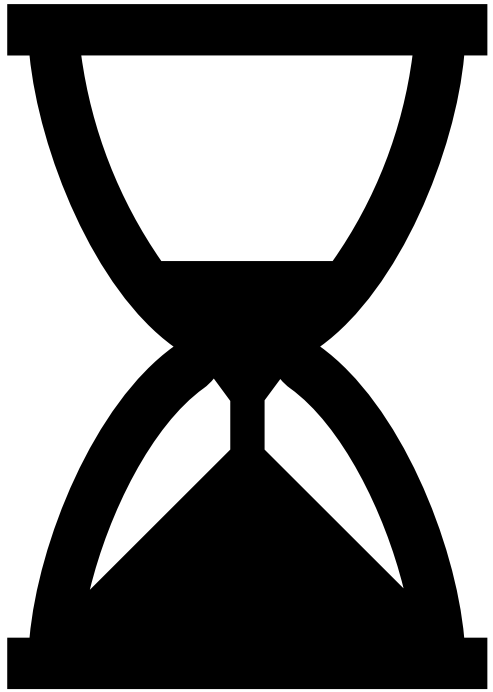
DURATION OF THERAPY

Bottom Line:

- It is reasonable to try to taper and discontinue HT around the age of 60 years.
- If needed (for persistent VMS, protection against bone loss/fracture, or personal preference), HT can be continued longer assuming she has had no changes in her personal or family history that substantially alter her risk.
  - Use transdermal route and lowest effective dose
  - Review regularly and use shared decision-making
- Discussions about duration of therapy do not apply to treatment of GSM with low dose estrogen therapies



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QUESTIONS & DISCUSSION

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