

Key Points: NAMS July 2008 Position Statement on Hormone Therapy

The North American Menopause Society.
Estrogen and progestogen use in postmenopausal women: July 2008 position statement of The North American Menopause Society. *Menopause* 2008.

This NAMS position statement has been endorsed by the American Medical Women's Association, The Endocrine Society, the National Association of Nurse Practitioners in Women's Health, the National Women's Health Resource Center, and the Society for Obstetricians and Gynaecologists of Canada.





Consistent Terminology Urged

- ET—Estrogen therapy
- EPT—Combined estrogen-progestogen therapy
- HT—Hormone therapy (encompassing both ET and EPT)
- Progestogen—Encompassing both natural progesterone and synthetic progestins

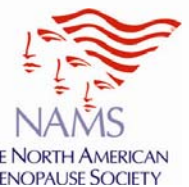
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Consistent Terminology Urged (cont'd)

- Natural/spontaneous menopause—The final menstrual period (FMP), confirmed after 12 consecutive months of amenorrhea with no obvious pathologic cause
- Induced menopause—Permanent cessation of menstruation after bilateral oophorectomy or iatrogenic ablation of ovarian function
- Perimenopause/menopause transition—Span of time when menstrual cycle and endocrine changes occur a few years before and 12 months after the FMP resulting from natural menopause

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Consistent Terminology Urged (cont'd)

- Premature menopause—Menopause reached at or under age 40, whether natural or induced
- Premature ovarian failure—Ovarian insufficiency experienced under age 40, leading to permanent or transient amenorrhea

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Consistent Terminology Urged (cont'd)

- Early menopause—Natural or induced menopause that occurs well before the average age of natural menopause (51 y), at or under age 45
- Early postmenopause—The time period within 5 y after the FMP resulting from natural or induced menopause



HT & Vasomotor Symptoms

- Treatment of moderate to severe vasomotor symptoms (ie, hot flashes, night sweats) remains primary indication for systemic HT
- Every systemic ET and EPT product approved for this indication in US/Canada



HT & Vaginal Symptoms

- ET is most effective treatment for moderate to severe symptoms of vulvar and vaginal atrophy
- Many systemic ET and EPT products and all local vaginal ET products approved in US/Canada for treating these symptoms
- Local vaginal ET generally recommended when HT is considered solely for this indication



HT & Sexual Function

- Treatment of moderate to severe vaginal atrophy with systemic ET/EPT or local ET can relieve dyspareunia, a common cause of intercourse avoidance
- One oral systemic ET product FDA approved for dyspareunia
- HT not recommended as sole treatment of other sexual function problems (eg, diminished libido)



HT & Urinary Health

- Local ET may benefit some women with urge incontinence who have vaginal atrophy
- Unclear if ET by any route is effective for overactive bladder
- Controversial if local ET can improve stress incontinence (systemic ET may worsen or provoke it)
- Local vaginal ET may reduce risk of recurrent UTI
- No HT product approved for urinary health in US/Canada



HT & Body Weight/Mass

HT has not been shown to affect:

- weight gain
- body mass index



HT & Quality of Life

- HT can improve health-related QOL through mood elevation and decreased menopause symptoms
- Unknown if HT improves health-related QOL in asymptomatic women
- HT not approved for this indication



HT & Osteoporosis

- HT proven to reduce postmenopausal osteoporotic fractures
- Many systemic ET-containing products approved for prevention of postmenopausal osteoporosis through long-term treatment
- Extended use of HT is option for women with low bone mass, regardless of menopause symptoms, when alternate therapies not appropriate



HT & Coronary Heart Disease

- HT may reduce CHD risk when initiated in younger and more recently postmenopausal women
- Longer HT duration associated with reduced CHD risk and mortality
- Some evidence of lower CHD risk in women who used HT ≥ 5 y

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HT & Coronary Heart Disease (cont'd)

- Short-term HT may increase CHD risk in women farther from menopause at time of initiation
- Long-term HT associated with less accumulation of coronary artery calcium
- HT currently not recommended as sole or primary indication for coronary protection in women of any age



HT & Stroke

- Both ET and EPT appear to increase ischemic stroke risk and have no effect on hemorrhagic stroke risk in postmenopausal women
- HT cannot be recommended for primary or secondary prevention of stroke



HT & Venous Thromboembolism

- Oral HT increases VTE risk in postmenopausal women
- VTE risk emerges soon after HT initiation (1-2 y) and decreases over time
- Lower VTE risk with either EPT or ET in women <60 y
- Possible lower VTE risk with transdermal than with oral ET
- Lower HT doses may be safer than higher doses
- Risks fall into the “rare” category



HT & Diabetes Mellitus

- HT reduces new DM onset
- Inadequate evidence to recommend HT for sole or primary indication for DM prevention in peri- or postmenopausal women
- Transdermal ET may have advantages over oral route in women with DM



HT & Endometrial Cancer

- Unopposed systemic ET associated with increased endometrial cancer risk related to dose and duration of use
- Standard-dose systemic ET for >3 y associated with up to 5-fold increased risk
- Adequate concomitant progestogen recommended for women with intact uterus
- Limited evidence for HT use with early-stage endometrial cancer history



HT & Breast Cancer

- Breast cancer risk increases with EPT use beyond 3-5 y
- Increased absolute risk of EPT in WHI viewed as “rare” (4-6 additional cases/10,000 women/y of EPT for ≥ 5 y)
- Unclear whether EPT risk differs between continuous and sequential progestogen use
- WHI ET trial showed no increased risk after 7.1 y (6 fewer cases/10,000 women/y of ET use; not statistically significant)
- ET for < 5 y has little impact on breast cancer risk

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HT & Breast Cancer (cont'd)

- EPT and, to a lesser extent, ET, increase breast cell proliferation, breast pain, and mammographic density
- EPT may impede diagnostic interpretation of mammograms
- Whether to use HT when history of breast cancer is unresolved (limited epidemiologic evidence mixed; no completed long-term RCTs)



HT & Mood/Depression

- Evidence mixed on HT mood effects when no clinical depression
- Insufficient evidence to support HT for treating depression
- Progestogens in EPT may worsen mood when a history of premenstrual syndrome, premenstrual depressive disorder, or clinical depression
- Controversial if ET augments antidepressant effects of SERMs



HT & Cognitive Aging/Decline, Dementia

- HT not recommended at any age for the sole or primary indication of preventing cognitive aging or dementia
- HT seems to increase dementia incidence when initiated at ≥ 65
- Inadequate data if HT started soon after menopause increases or decreases later dementia risk
- Limited data do not support HT for Alzheimer's disease



HT & Premature Menopause, Premature Ovarian Failure

- Inadequate data about HT use in premature menopause (≤ 40 y) or POF
- Most data suggest HT has protective CHD effect in these women
- Data regarding HT in women experiencing menopause at the typical age should not be extrapolated to these women
- Likely that risks attributable to HT are smaller and benefits greater in these younger women, but no trial data exist



HT & Total Mortality

- HT may reduce total mortality when initiated soon after menopause
- Both ET and EPT may reduce total mortality by 30% when initiated in women <60 y
- HT not associated with mortality reduction among women who initiate HT at ≥ 60 y



Class vs Specific Product Effect

- Estrogen and progesterone agonists share some common features/effects and have potentially different properties
- Only RCTs can determine an agent's net clinical outcome
- But without RCTs, data for one agent can be generalized to all agents within same hormonal family



Progestogen Indication

- Primary menopause-related indication for progestogen is endometrial protection from systemic ET
- Adequate progestogen recommended for women with an intact uterus using systemic ET
- Progestogen generally not indicated with local, low-dose ET for vaginal atrophy



HT Dosages

- Therapeutic goal is lowest effective estrogen dose (plus corresponding low progestogen dose for women with a uterus) consistent with individual treatment goals
- Lower doses better tolerated, may have more favorable benefit-risk ratio than standard doses (but lower doses have not been tested in long-term trials)
- Additional local ET may be needed for persistent vaginal symptoms



HT Starting Dosages

Lower daily doses typically used with systemic ET:

- 0.3 mg oral CE
- 0.5 mg oral micronized 17β -estradiol
- 0.014-0.025 mg transdermal 17β -estradiol patch

Typical lowest doses of progestogen:

- 1.5 mg oral MPA
- 0.1 mg oral norethindrone acetate
- 0.5 mg oral drospirenone
- 50-100 mg oral micronized progesterone



HT Routes of Administration

- No clear benefit of one route of administration for systemic ET
- Nonoral routes may offer both advantages and disadvantages compared with oral route
- Transdermal ET may be associated with lower DVT risk than oral route (observational data, not RCTs)
- Local ET preferred when solely vaginal symptoms
- Systemic progestogen required for endometrial protection from unopposed systemic ET



EPT Regimens

- When adding progestogen to estrogen for endometrial safety, multiple approved dosing options available
- Inadequate research to endorse one EPT regimen over another
- Current data support minimizing progestogen exposure

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EPT Regimens (cont'd)

Insufficient evidence regarding endometrial safety to recommend:

- Off-label use of long-cycle regimens
- Vaginal administration of progesterone
- Levonorgestrel-releasing intrauterine system
- Low-dose estrogen without progestogen



Bioidentical Hormone Therapy

- Many well-tested brand-name products containing "BHT" approved in US/Canada
- But term "BHT" typically used to mean custom-made HT formulations compounded for an individual according to a healthcare provider's prescription
- Custom "BHT" may provide doses, ingredients, and routes of administration not commercially available
- Salivary hormone testing often used to adjust custom "BHT" levels, but FDA says no scientific basis

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Bioidentical Hormone Therapy (cont'd)

- Not tested for efficacy, safety, batch standardization, purity
- Individual formulation not approved by any regulatory agency
- FDA says that compounding pharmacies make false and misleading claims about safety and effectiveness
- NAMS recommends "BHT" products carry patient package inserts explaining benefits and risks identical to those required by approved HT products



Evaluation Prior to HT Initiation

- Comprehensive history and physical evaluation essential
- Mammography within the 12 months before HT initiation
- Other special examinations (eg, bone densitometry) on case-by-case basis



Timing of HT Initiation

- Initiation in relation to proximity to menopause seems to have strong impact on long-term health outcomes
- For example, early HT initiation may reduce total mortality and CHD risk

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Timing of HT Initiation (cont'd)

- Women >60 y who had natural menopause at typical age and never used HT should not start HT without compelling indication/counseling
- HT should not be recommended for younger women who had premature menopause or POF until they reach typical age of menopause (51 y)



Individualization of Therapy

- An individual risk profile is essential when contemplating HT
- Each woman must be informed of her known risks
- Acceptance of HT risks varies with the individual
- Acceptance of HT risks varies as to primary indication (eg, relieve existing symptom or prevent disease later on)

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Individualization of Therapy (cont'd)

- Benefit-risk ratio more acceptable for short-term symptom relief in a younger population
- Long-term HT or HT initiation in older women less acceptable
- Women with premature menopause have increased symptoms and risks
- Recommendations vary for first users versus previous users in their 60s



HT Duration of Use

- No clear indication that longer HT duration improves or worsens the benefit-risk ratio
- HT effects on long-term risks have not been studied in perimenopausal women
- Thus, findings from RCTs of postmenopausal women should be extrapolated with caution for younger women

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HT Duration of Use (cont'd)

Extending HT use is acceptable:

- For women well aware of potential risks and benefits
- With lowest effective dose
- For further prevention of osteoporotic fracture and bone loss when alternate therapies not appropriate
- With clinical supervision



HT Discontinuance & Symptom Recurrence

- 50% chance of symptoms recurring when HT discontinued
- Vasomotor symptom recurrence similar whether tapered or abrupt discontinuance
- Data conflicting regarding breast cancer incidence after discontinuance
- Decision to resume HT must be individualized



Explaining Risk

- Essential to understand basic concepts of risk and be able to explain risk to patients
- Tailor the discussion to the individual patient
- Be sensitive whether she wants numerical information, your honest opinion, or both
- Providing figures for absolute risk is clearer than relative risk
- Put the risk in perspective (ie, a risk is “rare” if it occurs ≤ 10 per 10,000 patients per year; it’s “very rare” if it occurs ≤ 1 per 10,000 per year)



Explaining HT Risk

- Potential absolute risks for use of HT are low, especially for ET in WHI
- In WHI, risks for EPT were “rare,” except for stroke
- For younger women (<50 y) or those at low risk of CHD, stroke, osteoporosis, breast cancer, or colon cancer, absolute risk or benefit is likely to be even smaller than seen in WHI
- Each regimen, route of administration, and timing of therapy has distinct beneficial and adverse effects

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Explaining HT Risk (cont'd)

HT risk is related to:

- A woman's baseline disease risks
- Her age
- Age at menopause
- Cause of menopause
- Time since menopause
- Prior use of any hormone
- HT types, routes of administration, and doses used
- Emerging medical conditions during treatment



Summary

- The HT benefit-risk ratio continually changes with woman's age and menopause-related symptoms
- Ratio is more favorable close to menopause, but decreases with aging and time since menopause in previously untreated women

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Summary (cont'd)

- Recent data support HT initiation around the time of menopause to:
 - Treat menopause-related symptoms and/or
 - Treat or reduce the risk of certain disorders (eg, osteoporosis or fractures) in select postmenopausal women
- HT use should be consistent with treatment goals, benefits, and risks for the individual woman