North American Menopause Society (NAMS)

2012 Hormone Therapy Position Statement

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NAMS position statement. *Menopause* 2012.

Definitions

ET = estrogen (only) therapy

EPT = estrogen + progestin therapy

HT = ET and EPT

BENEFITS & RISKS OF HORMONE THERAPY

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BENEFITS & RISKS OF HORMONE THERAPY

Treatment of Symptoms

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HT & Vasomotor Symptoms

- HT is the most effective treatment of menopause-related vasomotor symptoms
- Almost all systemic HT products are approved for vasomotor symptom relief

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HT & Quality of Life

- Although HT is not approved for enhancing QOL, HT can improve health-related QOL in *symptomatic* women
- Unclear if HT improves health-related QOL in *asymptomatic* women

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HT & Vaginal Symptoms

- ET is the most effective treatment of moderate to severe symptoms of vulvar and vaginal atrophy
- Many systemic HT and local vaginal ET products (tablets, creams, rings) are available for treating the symptoms of atrophy

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BENEFITS & RISKS OF HORMONE THERAPY

Osteoporosis

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HT & Osteoporosis

- HT reduced the risk for fracture (eg, hip, spine, nonspine) in postmenopausal women in the Women's Health Initiative (WHI) who were not selected on the basis of osteoporosis
- Many systemic HT products are approved for *preventing* postmenopausal osteoporosis
- No HT product is approved for *treating* osteoporosis

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BENEFITS & RISKS OF HORMONE THERAPY

Cardiovascular Disease and VTE

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HT & Osteoporosis (cont'd)

- Benefits of HT on bone mass dissipate quickly after discontinuation
- Extended use of HT is an option for women at high risk of osteoporotic fracture if alternate therapies are contraindicated *however*, the risks of long-term HT use should be considered

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HT & Coronary Heart Disease

- ET may reduce CHD and coronary artery risk when initiated in younger and more recently postmenopausal women without a uterus
- HT is currently *not* recommended for coronary protection in women of any age

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HT & Stroke

- Both ET and EPT appear to increase ischemic stroke risk but have no effect on hemorrhagic stroke risk

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BENEFITS & RISKS OF HORMONE THERAPY

Cancer

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HT & Venous Thromboembolism

- Oral HT increases the risk of VTE in postmenopausal women
- The VTE risk emerges soon after HT initiation (1-2 y) and decreases over time
- Some studies suggest a lower VTE risk with transdermal and lower doses of oral HT, but there is no current RCT evidence available

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HT & Endometrial Cancer

- Unopposed systemic ET in postmenopausal women with an intact uterus is associated with increased endometrial cancer risk related to dose and duration of use
- HT not recommended in a patient with a history of endometrial cancer

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HT & Breast Cancer

- The diagnosis of breast cancer increases with EPT use beyond 3-5 years
- It is unclear whether EPT risk differs between continuous and sequential progestogen
- EPT and to a lesser extent ET increase breast cell proliferation, breast pain, and mammographic density
- EPT may impede diagnostic interpretation of mammograms

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HT & Breast Cancer (cont'd)

- ET arm of WHI showed no increased cancer risk after a mean of 7.1 years on study
- ET and EPT use in breast cancer survivors may increase recurrence risk

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HT & Breast Cancer (cont'd)

- Breast cancer diagnosis dissipated 3 years post EPT cessation
- Breast cancer mortality was higher in women assigned to EPT compared to placebo
- Women starting EPT shortly after menopause experience increased breast cancer risk, but those with a gap time greater than 5 years do not

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HT & Ovarian Cancer

- Data on HT and risk of ovarian cancer are conflicting
- There were increases of ovarian cancer in those using EPT in WHI but the numbers did not reach statistical significance

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HT & Lung Cancer

- There was no significant increase in the incidence of non-small-cell lung cancer with EPT over 7.1 years of intervention in the WHI
- Lung cancer mortality was higher with EPT use
- No increase in incidence or mortality was seen with ET

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HT & Cognitive Aging/Dementia

- Evidence is mixed on the effect of HT on cognition at time of menopause
- There is no effect on episodic memory or executive function with ET at time of menopause
- The WHI Memory Study reported an increase in dementia with HT use at ages 65-79
- HT not recommended at any age for preventing or treating cognitive aging or dementia

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BENEFITS & RISKS OF HORMONE THERAPY

Dementia

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Therapeutic Pearls

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HT & Premature Menopause/ Premature Ovarian Insufficiency

- The data regarding HT in women over age 50 should not be extrapolated to younger postmenopausal women
- It is likely that risks attributable to HT are smaller and benefits greater in these younger women
- Use of HT or oral contraceptives until the median age of menopause is recommended at which time the decision can be reevaluated

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Progestogen Indication

- The primary menopause-related indication for protestogen use is endometrial protection from systemic ET
- Therefore, adequate progestogen is recommended for women with an intact uterus using systemic ET
- Progestogen is generally not indicated with low-dose local ET for vaginal atrophy

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Class vs Specific Product Effect

- All estrogens share some common features but may have unique properties as well (look for upcoming KEEPS trial data comparing oral and transdermal estrogens)
- Same is true for progestogens
- Without RCTs, data for one agent should be generalized to all agents within same hormonal family
- More research required

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Dose & Route of Administration

- The therapeutic goal is to use the lowest effective estrogen dose consistent with individual treatment goals, benefits, and risks, plus appropriate progestogen dose for women with a uterus
- Lower doses have fewer side effects and may have more favorable benefit-risk ratio than the standard doses used in the WHI but lower doses not been tested in long-term trials

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Bioidentical Hormone Therapy (BHT)

- "BHT" usually refers to custom-compounded formulations
- Custom BHT may combine several hormones and use nonstandard routes of administration
- Use of compounded BHT and salivary hormone testing are not recommended
- BHT is not tested for efficacy, safety, batch standardization, or purity

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Conclusions & Recommendations

- Individualization is the key in decisions to use HT and should incorporate the woman's health and QOL priorities as well as her personal risk factors for VTE, CHD, stroke, and breast cancer

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Bioidentical Hormone Therapy (cont'd)

- FDA says that compounding pharmacies make false and misleading claims about the safety and effectiveness of BHT
- BHT should include package inserts explaining the benefits & risks just like government-approved HT products
- Compounded HT should only be used by women allergic to ingredients in approved products
- Many well-tested, government-approved, brand-name HT products contain hormones chemically identical to those made by ovaries

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Conclusions & Recommendations (cont'd)

- Duration of use recommendations differ for EPT and ET:
  - For EPT, the duration is limited by the increased risk of breast cancer and breast cancer mortality associated with more than 3-5 years of use
  - For ET, the more favorable benefit-risk profile during a mean of 7 years of use and 4 years of follow-up allows more flexibility in the duration of use

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Conclusions & Recommendations (cont'd)

- ET is the most effective treatment for vulvar and vaginal atrophy; low-dose local vaginal ET is advised when only vaginal symptoms are present
- Women with premature or early menopause can use HT until the median age of menopause (51 y); longer duration can be considered for symptom management

NAMS position statement. *Menopause* 2012. (cont'd)

North American Menopause Society (NAMS) - 2012 Hormone Therapy Position Statement

The Position Statement can be downloaded from the following location on www.menopause.org:

http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2

NAMS position statement. *Menopause* 2012.

A Decade After The Women's Health Initiative— The Experts Do Agree

- The statement was published in the journals of The North American Menopause Society (*Menopause*), the American Society for Reproductive Medicine (*Fertility and Sterility)*, and The Endocrine Society (*Journal of Clinical Endocrinology and Metabolism*)

Stuenkel, et. al. *Menopause* 2012; 19(8): 846-847.

Well-Woman Care: New(er) Recommendations for Old(er) Women

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- American Congress of Obstetricians and Gynecologists
- U.S. Preventive Services Task Force
- American Society for Colposcopy and Cervical Pathology
- American College of Radiology
- American Cancer Society
- National Osteoporosis Foundation

Cervical cancer screening

Objectives

- Review recent revisions in guidelines from national colleges as they pertain to women of menopausal age
- Provide rationale for changes in protocol
- Be able to provide age appropriate counseling for women regarding routine health screening

Cervical cancer screening

- New guidelines from ACS, ASCCP, ASCP and ACOG (2012)
- Women age 30 – 65
  - Screen with cytology and high risk HPV testing every 5 years (preferred)
  - Screen with cytology alone every 3 years
  - More frequent for immunocompromised women, DES exposure or prior high grade dysplasia/ cancer

Cervical cancer screening: Rationale for changes

- Better understanding of HPV oncogenicity
- Slow rate of progression from infection to dysplasia to cancer
- High cost of false positive testing
- Increased sensitivity of co-testing for detecting CIN 3 or greater

Cervical cancer screening Rationale for changes

- Cervical cancer occurs average of 15 – 25 years after HPV infection
- Continuing screening to age 90 would prevent 1.6 cases/ 1000 women at high cost
- Epithelial atrophy leads to high false positive rate

ACOG Practice Bulletin # 131, November 2012

Cervical cancer screening Over age 65

- Discontinue screening:
  - If 10 years of prior negative screening
  - No treatment of high grade dysplasia or AIS in last 20 years
  - Do not restart even with new sexual partner

Cervical cancer screening Post-hysterectomy

- Discontinue screening:
  - If no history of high grade dysplasia or cancer
  - No need for prior negative screening
  - Do not restart even for new sexual partner

Pelvic exam

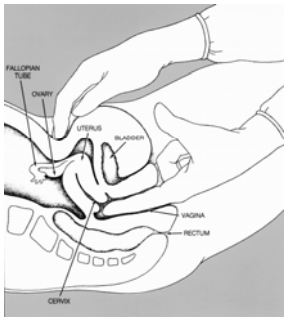

Image used is in the public domain (Original source National Cancer Institute).

Pelvic Exam

- Without symptoms?
  - "No evidence supports or refutes the annual pelvic examination… for the asymptomatic low-risk patient."
  - May stop annual assessments when age/ health would preclude intervention for conditions detected on exam

ACOG Committee Opinion #534, August 2012

Pelvic Exam

- Always appropriate in symptomatic patient
- Common problems in menopausal women:
  - Vaginal dryness
  - Symptoms related to prolapse
  - Urinary or fecal incontinence
  - Suspected vaginal bleeding

Pelvic Exam

- Following hysterectomy/ BSO
  - Internal exam may be deferred if asymptomatic
  - Exceptions:
    - History of cervical cancer or high grade dysplasia
    - HIV infection
    - DES exposure in utero
  - Annual exam of external genitalia should continue

Breast cancer screening

Image from Wikipedia

Why the difference?

- USPSTF acknowledges that studies demonstrate reduction in mortality age 39-69
- But number of tests required to prevent one death much higher in 39-49 y/o group
- Most RCTs reviewed for metaanalysis involved biennial screen; no meaningful comparison between screening strategies

Mammography

- Age 40 years and older annually
  - American College of Ob/Gyn
  - American Cancer Society
  - Nat'l Comprehensive Cancer Network
- Age 50 – 74 years every other year
  - US Preventive Services Task Force (2009)

Mammography

USPSTF guideline (Ann Intern Med 2009; 151:727)

"The decision to start … screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms."

Examples of harms:

Psychological harm	Unnecessary visits
Unnecessary biopsies	Additional radiation exposure

Mammography
When to stop?

USPSTF (2009): Age 75

ACOG (2011): Decision to be made in consult with MD, taking into account comorbidities and life expectancy

- Benefit of screening decreases compared w/harms of overtreatment with advancing age
- Most clinical trials examined had upper age limit 64 – 74 years

Clinical Breast Exam

- Increases sensitivity in detecting cancer over mammography alone (88.6% → 94.6%)
- Also increases false positive rate (7.4% → 12.4%)

Chiarelli et al, J Natl Cancer Inst 2009; 101:1236-43

Clinical Breast Exam

- Age 40 years and older annually
  - American College of Ob/Gyn
  - American Cancer Society
  - Nat'l Comprehensive Cancer Network
- Not recommended
  - US Preventive Services Task Force

Breast self-exam

- USPSTF and NCI recommend against
  - Teaching BSE does not reduce mortality, but is associated with harms "that are at least small"
- ACOG and ACS recommend "breast self-awareness"
  - Defined as awareness of the normal appearance and feel of the breasts
  - Can include breast self-examination

Osteoporosis

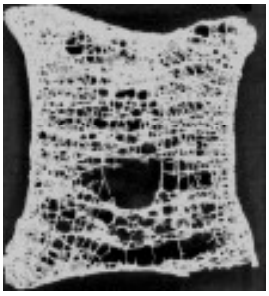

Image provided courtesy of Welcome Images

Osteoporosis screening

- Fracture Risk Assessment Tool (FRAX)
  - Developed in collaboration with WHO
  - Predicts risk of osteoporotic fracture within 10 yrs
  - Takes into account multiple clinical risk factors
  - Found at: http://www.sheffield.ac.uk/FRAX/
- 10 year risk in 65 y/o Caucasian woman with no other risk factor = 9.3%

Osteoporosis screening

- USPSTF (2011): Age 65 and older
  - Age < 65 if fracture risk ≥ 65 y/o with no other risk factors
- ACOG (2012): Age 65 and older
  - Age < 65 if other risk factors are noted
    - Hx of fracture
    - Smoker
    - Alcoholism
    - Thin, frail
    - Medications causing bone loss

Osteoporosis screening

- How often to screen?
- If no increased risk of fracture in woman >65:
  - Normal BMD or T score ≥ -1.5 — 15 years
  - T score -1.5 - -1.99 — 5 years
  - T score -2.0 - -2.49 — 1 year

ACOG Practice Bulletin #129, September 2012

Helpful websites

- www.uspreventiveservicestaskforce.org
- www.acog.org/wellwoman
- www.cancer.org/healthy/findcancerearly/index

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