

# Understanding and Explaining Hormone Therapy Risk

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The 2008 position statement of The North American Menopause Society (NAMS) regarding recommendations for menopausal hormone therapy (HT) for postmenopausal women considers the current best practice of medicine from a clinical perspective. The undue fear and confusion generated in recent years by overextrapolation or misinterpretation of clinical studies mandate a clearer explanation of the therapeutic benefit-risk ratio of HT for women at various times through menopause and beyond, and of how these benefits and risks influence both healthcare providers and the women weighing the use of such therapy.

## Explaining HT Risk

Risk is actually a very difficult concept to understand. It is also open to abuse and misinterpretation. Yet the decision a woman faces to use hormones or not, if clinically indicated, is entirely based on her concept of risk and how the data are presented to her.

Studies comparing outcomes with exposures attempt to identify or calculate the degree to which the outcome is associated with the exposure. But a statistical association between an exposure and an outcome does not necessarily mean that the exposure caused the outcome. A weak association or an association found only in a single study, particularly if it is not a randomized controlled trial, should

not be taken as concrete evidence of a true cause-and-effect relationship.

## Practical Considerations of the NAMS Position Statement

HT should only be considered if there is a legitimate indication, the woman has been fully evaluated, and there is a clear understanding of both the potential benefits and the potential risks.

*Vasomotor symptoms.* Systemic estrogen therapy (ET) or combined estrogen-progestogen therapy (EPT) for women with an intact uterus is the gold standard for treatment of vasomotor symptoms (hot flashes and night sweats) and, hence, is the drug of choice, provided there is no reason not to prescribe.

*Vaginal symptoms.* The cause of vaginal atrophy is estrogen deficiency, and the most appropriate treatment is local ET. Low-dose intermittent application of local ET is exceptionally safe and there is little evidence for adverse effects.

*Sexual function.* Local ET is helpful for relief of dyspareunia (painful intercourse). There is little evidence that ET or EPT will aid sexual desire disorder, so this is not an indication for HT.

*Urinary health.* In the presence of vaginal atrophy, local ET is recommended for symptoms of frequency and urgency in the absence of painful urination. There is no evidence to support HT for the alleviation of true stress urinary incontinence.

*Change in body weight/mass.* HT usage is not a cause of weight gain.

*Quality of life.* There is good evidence for an improvement in health-related quality of life in symptomatic women treated with HT.

*Osteoporosis.* There is little doubt that HT reduces bone loss and fractures, even in women who were not bone deficient at the time of commencing therapy. Whether HT is prescribed for this indication, however, is one of the biggest challenges facing a clinician.

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*This article is a brief synopsis of a comprehensive Web-based CME/CE activity that discusses the 2008 hormone therapy position statement from The North American Menopause Society (NAMS). This activity, called a Clinical Update, was developed in connection with a collaboration among Medscape, NAMS, and the National Association of Nurse Practitioners in Women's Health, and is supported by an educational grant to Medscape from Wyeth. The Clinical Update can be accessed through the NAMS Web site at [www.menopause.org/MS.aspx](http://www.menopause.org/MS.aspx).*

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*Coronary heart disease.* Women who reach menopause at the typical age and who start HT within no more than 5 years of menopause are likely to gain some protection against coronary heart disease. But starting HT 10 or more years beyond menopause will likely increase this risk. The absolute risks, however, are rare.

*Stroke.* The EPT and ET trials in the Women's Health Initiative (WHI) demonstrated an increased risk of ischemic stroke.

*Venous thromboembolism.* HT increases the risk of venous thromboembolism (VTE) for women, but the level of risk is rare. Growing evidence suggests that women with a prior history of VTE or women who possess factor V Leiden are at increased risk for VTE with HT use.

*Diabetes mellitus.* Having diabetes mellitus (DM) is not a contraindication for HT. When prescribing estrogen for a woman with DM, nonoral preparations may be preferred because of their reduced impact on raising triglycerides.

*Endometrial cancer.* Unopposed estrogen (ET) significantly increases the incidence of endometrial cancer in women with an intact uterus. With rare exceptions, these women must receive concomitant progestogen to reduce the risk to the level of not using ET.

*Breast cancer.* HT and the risk of breast cancer is a cause of concern to women. With EPT in the WHI, use beyond 5 years is associated with increased risk, even though the absolute risk falls into the rare category. With ET, there was no increase in risk after an average of 7.1 years of use.

*Mood and depression.* ET can enhance the sense of well-being, but

## Counseling Women Using Data

Using data to explain HT risks can be extremely helpful, but it can also be very confusing. Some tips:

- Say that 2 of every 10 women experience the side effect— not that there is a 20% chance of a side effect.
- Use the same denominator, such as 1,000 or 10,000 (eg, "Headache developed in 12 of every 1,000 women without the drug, compared to 20 of 1,000 women with the drug").
- Recognize that even in the absence of an exposure (eg, HT use), there is a risk of developing the disease under consideration.
- Be careful not to overstate the risk, especially if the studied population has a low rate.
- Recognize that a woman's values, education, needs, preferences, and emotions affect the way she considers risk, so data alone may not influence her.
- Understand that different adverse health outcomes may have the same risk, but women may fear certain outcomes more than others.
- Recognize that media reports of new medical research can lead to misunderstanding of the reported risks, often due to the practice of delivering news in small, incomplete portions.
- Be sensitive as to whether a patient seeks numerical information, your honest professional opinion, or both.

there is no evidence to justify use of HT as an antidepressant. Progestogens may actually induce symptoms similar to premenstrual syndrome.

*Cognitive aging/decline and dementia.* There is little evidence that HT use restores memory or prevents or treats Alzheimer's disease.

*Premature menopause and premature ovarian failure.* Limited evidence favors these women being prescribed HT, at least up to the typical age of menopause (51 years). Thereafter, the factors affecting the decision to continue HT become the same as for all other women.

*Total mortality.* HT may reduce total mortality when initiated soon after menopause.

*Individualization of therapy is key.* Individualization is what the art of menopause management is all about.

Know the data, help women understand risk, and weigh the level of potential risk and benefit for her personal circumstances.

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