Managing Menopausal Hormone Therapy in 2016

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Session Objectives

• Discuss the event of menopause
• Describe and identify common symptoms experienced by women around the time of menopause
• Identify major studies that provide an evidence-based framework with which to discuss Menopause
• Develop approaches to treatment options for menopausal women factoring in patient preferences, treatment options, and risk-benefit considerations
  - lifestyle changes
  - over-the-counter remedies
  - prescription therapy
• Discuss ongoing challenges still to be resolved regarding menopausal care

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Recommendations for Clinical Care

• “Unique opportunity for a dialogue between women and their healthcare providers to evaluate and improve health-related practices”.  [Level II]

• “Menopause counseling, including discussion of physiologic changes, assessment of menopause-related symptoms and treatment options, review of screening recommendations, and discussion of disease risk-reduction strategies and psychosocial issues, facilitates informed decision making among midlife and older women”.  [Level II]

• “By considering women’s concerns, values, and preferences, menopause practitioners have the potential to enhance women’s sense of well-being, not only at menopause but for the remainder of their lives”.  [Level III]

The North American Menopause Society Recommendations for Clinical Care of Midlife Women. (2014)

How women view menopause

• Midlife women do not consider menopause a time of health complaints, increased disease risk or a time for medical care, but rather a normal developmental phase

• 51% in early postmenopause said they were happier and more fulfilled than in their 20s, 30s, or 40s

• About 75% of women surveyed reported making some kind of lifestyle change at menopause

• In a survey of 12,275 perimenopausal women about their attitudes toward menopause, the mean score for all ethnic groups studied was positive.

• Women with negative attitudes toward menopause report more menopausal symptoms

From: Menopause 2010; Woods Menopause 1999; NAMS/Gallup Survey Menopause 1999; Sommer Psychosomatic Medicine 1999;
Framework

• STRAW + 10
  Stages of Reproductive Aging Workshop

• SWAN
  Study of Women’s Health Across the Nation

• WHI
  Women’s Health Initiative

- WHI Secondary Analyses

Definition of Menopause

• Normal Physiologic Event
• Defined as Final Menstrual Period (FMP), reflecting loss of ovarian follicular function
• Spontaneous/Natural Menopause recognized retrospectively with absence of menses for 12 consecutive months
• Average age: 52 but can vary widely
• Induced menopause refers to cessation of menstruation that occurs after either bilateral oophorectomy or iatrogenic ablation of ovarian function (e.g., by chemotherapy or pelvic radiation).
• No Clinical Biological Markers during PeriMenopause (STRAW + 10: “Lack of standardized assays for key biomarkers remains an important limitation in efforts to stage reproductive aging and to translate research findings to cost-effective clinical tools”...ovarian markers of reproductive aging including: antimullerian hormone, inhibin-B, follicle-stimulating hormone, and antral follicle count.)
• Permanent end of fertility

There is no one universal menopausal syndrome

North American Menopause Society, Clinical Care Recommendations 2014

The Stages of Reproductive Aging Workshop: STRAW + 10

- Established a nomenclature and staging sx for female reproductive aging continuum in 2001, revised in 2011 with STRAW + 10 staging sx.
- Term menopause transition refers to span of time when menstrual cycle and endocrine changes occur, beginning with variation in the length of the menstrual cycle and ending with the FMP.
- Provides a more comprehensive basis for assessing reproductive aging in research and clinical contexts
Other Definitions:

- **Primary Ovarian Insufficiency**
  - Transient or permanent loss of ovarian function leading to amenorrhea in women aged younger than 40 years.
  - Affects approximately 1% of women.

- **Early Menopause**
  - Menopause occurring in women aged 40 to 45 years
  - Experienced by approximately 5% of women.

- **Premature Menopause**
  - Definitive cases of menopause before age 40, such as with the surgical removal of both ovaries.

“**We want to add **
life
**to years,**
not just add years to life.”

Robert Reid, Author

Menopause is:

- Multi-Dimensional Event often perceived differently across cultures
  - Psycho-Social/Developmental changes
  - Biological responses
  - Hot Flashes & Night Sweats
  - Sleep Quality & Quantity
  - An Emotional roller coaster
  - Cardiovascular Concerns
  - Bone loss
  - Fatigue & Cognitive changes
  - Sexual health
  - Urogenital symptoms
  - Skin changes

There is no one universal menopausal syndrome
**SWAN**

- **Study of Women’s Health Across the Nation**
  - The study began in 1994 and is in its twenty-second year.
  - Between 1996 and 1997, 3,302 participants joined SWAN through seven designated research centers.
  - Longitudinal, multi-ethnic, community based observational study of women at midlife
  - 5 different ethnic groups
    - African-American
    - Caucasian
    - Chinese
    - Hispanic,
    - Japanese,


**Findings related to Diversity**

- There are racial and ethnic differences in the timing of menopause
- Hispanic and African-American women had greatest prevalence of premature and early menopause
- Japanese-American women reported the least amount of symptoms during this phase of reproduction.

  _Santoro & Green, Menopausal Medicine 2009_

**Other Symptoms**

- Vaginal symptoms: Hispanic women suffer more than any other group.
- Mood: Depressive symptoms were more likely in Hispanic and African-American women
- Mood least likely affected in Chinese and Japanese women.

  _Santoro & Green, Menopausal Medicine 2009_
Sleep

- Younger women (< 45) have more difficulty with sleep
- African-American and Hispanic have the most difficulty with sleeping
- Manifested as trouble staying asleep and early morning awakening.

Santoro & Green, Menopausal Medicine 2009

Addressing Patient Complaints at Menopause

- Changes in Uterine Bleeding
- Vasomotor Symptoms
- Vulvar Vaginal Atrophy (VVA), GenitoUrinary Syndrome of Menopause (GSM)
- Sexual Concerns

Changes in Uterine Bleeding

- Approximately 90% of women will experience menstrual changes 4-8 years before menopause
- Mostly due to decreased frequency of ovulation and erratic levels of hormones
- Menstrual changes in midlife women:
  - Lighter (32%)
  - Heavier (29%)
  - Longer (20%)
  - Shorter (24%)
  - Skipped menses

Mitchell, Woods, Manella, 2006
Vasomotor Symptoms

- Most common reason menopausal women seek care
- Associated with
  - Physiologic circulatory change
  - Transient decrease in regional brain flow
  - Diminished sleep quality, irritability
  - Difficulty Concentrating
- Average duration: 3 years, but 25% remained 5 years, and 10% lasted ≥ 10 years
  - SWAN
    - Average 7.4 years
    - Women with earlier onset had longest duration: median > 11.8 yrs
  - Longer duration: Younger; Lower educational level; greater perceived stress & symptom sensitivity; higher depressive sx or anxiety with first report of VMS
- In SWAN:
  - AA women: median of 10.1 years
  - Asian women: median 5 years

Freeman, 2011; Avis, 2015, SWAN
VulvoVaginal Atrophy

VIVA: (n=3520 postmenopausal women aged 55-65 years living in England, the United States, Canada, Sweden, Denmark, Norway, and Finland. 2012) asked women how does vaginal discomfort affect your life?

- 80% considered it to negatively affect their lives
- 75% reported negative consequences on sex life
- 68% reported that it makes them feel less sexual
- 36% reported that it makes them feel old
- 33% reported negative consequences on marriage/relationship
- 26% reported a negative effect on self esteem
- 25% reported that it lowers QOL

REVIVE: (n=3046 US women with sx of VVA. 2013)

Only 7% reported that their healthcare practitioner initiated a conversation about VVA and yet:

- 85% of partnered women had “some loss of intimacy”
- 59% indicated VVA sx detracted from enjoyment of sex
- 47% of partnered women indicated VVA interfered with their relationship
- 29% reported VVA had a negative effect on sleep
- 27% reported VVA had a negative effect on their general enjoyment of life


Physiology cont.

- Vagina loses elasticity, shortens, narrows, easily traumatized and irritated
- Loss of rugae, fornices become obliterated, cervix flush with vaginal vault
- Petechiae may be present
- pH greater than 5.0, parabasal cells replace normal vaginal epithelium
- Repopulation with diverse vaginal flora occurs, resulting in frequent UTIs

(NAMS, 2007)

Effects of Reinitiating Topical Estrogen Therapy
Hormone Therapy and Non-Pharmacological Interventions

Choosing an Intervention
Use an Evidence-Based Approach

- Pharmacological Interventions:
  - Hormonal
  - Non-hormonal (FDA approved & off label)
- Non-Pharmacological Interventions

The decision of which intervention to use is dependent upon various factors:
- Risk/Benefit Evaluation
- Patient Preference
- Costs of Intervention
- Side/Adverse Effects

Informed Consent Is a Process, Not a Form

Informed Consent Discussions Should Include
- The diagnosis and the nature of the condition
- The nature and purpose of the recommended treatment or procedure, including its risks and potential complications
- All reasonable alternative treatments or procedures, including the option of taking no action, and the risks of each option
- The relative probability of success for the treatment or procedure

Menopausal Management: An Evidence Based Approach


Consistent Terminology Urged

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

Class vs Specific Product Effect

- Estrogen and progesterone agonists share some common features/effects and have potentially different properties
- Without RCTs, data for one agent should be generalized to all agents within same hormonal family
- Theoretically, differences are likely but evidence required
Contraception in Menopause Transition

- Women of older reproductive age who do not wish to conceive should use effective contraception until 1 year >LMP (or usual age of menopause)
  - Guidelines from CDC represent a valuable resource (Level II)

- No contraceptive methods are contraindicated on the basis of age alone.
  - Combination hormonal contraceptives provide important non-contraceptive benefits, including
    - treatment of irregular uterine bleeding
    - reduction of vasomotor symptoms,
    - decreased risk of ovarian and endometrial cancer
    - maintenance of bone mineral density. (Level II)

Contraception in Menopause Transition

- Contraceptive methods that contain estrogen should be used with caution in women of older reproductive age who:
  - Smoke
  - Are Obese
  - Have other risk factors for cardiovascular disease. (Level II)

- Long-acting reversible contraceptive methods provide superior contraceptive effectiveness (Level I)
  - Copper IUD
  - Two levonorgestrel IUS
    - The higher-dose levonorgestrel IUS can be used as a first-line treatment for heavy menstrual bleeding and is an effective reversible alternative to endometrial ablation and hysterectomy.
  - Etonogestrel subdermal implant (Implanon)

Contraindications to Hormone Therapy

- Active liver disease
- Active or recent arterial thromboembolic disease (angina, MI)
- Current, past, or suspected breast cancer (systemic HT)
- Known hypersensitivity to active substance of the therapy
- Known or suspected estrogen sensitive malignant conditions
- Previous h/o of PE/DVT
- Undiagnosed genital bleeding
- Untreated endometrial hyperplasia
FDA-Approved Indications

- Relief of Moderate to Severe Vasomotor Symptoms (VMS)
- Genitourinary Syndrome of Menopause (GSM)
  - Bothersome symptoms of vaginal dryness and irritation
  - Vulvovaginal atrophy (VVA)
  - Dyspareunia
  - Some higher dose systemic MHT regimens are approved for VVA and many may resolve GSM while lower-dose regimens may be inadequate for the relief of vaginal sx
- Prevention of Osteoporosis

Estrogen Therapy And Estrogen-Progestogen Therapy

- Primary indication for HT: Treatment of moderate to severe vasomotor symptoms
  - The benefits outweigh the risks for most healthy, symptomatic women aged younger than 60 years or within 10 years of the final menstrual period.
- Types of therapies (ET, EPT, CEE/BZA) may have different side effects, benefits or risks.
  - Evidence from randomised, controlled trials is lacking.
  - A combination of SERM (TSEC) bazedoxifene with conjugated estrogen do not require a progestogen for uterine protection.
  - Both transdermal ET and low-dose oral ET have been associated with a lower risk of VTE and stroke compared with standard-dose oral ET in observational studies.

Hormone Therapy Management

- HT has a complex pattern of benefits and risks but is the most effective treatment for vasomotor symptoms associated with menopause at any age
- HT has a variety of effects that appear to be modified by age and/or time since menopause at initiation of MHT.
  - Benefits are more likely to outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause.
- Women have low absolute risks of chronic disease outcomes on MHT and risk stratification will help to identify women in whom benefits would be expected to outweigh risks.
- Findings from the intervention and extended post-intervention follow-up of the 2WHI HT trials do not support use for chronic disease prevention (Level I) (Manson et al. (2013). Menopausal Hormone Therapy and Health Outcomes During Intervention and Extended Post-Stopping Phase of the Women's Health Initiative Randomized Trials. JAMA.)
Hormone Therapy Management

- Estrogen as a single systemic agent is appropriate in women after hysterectomy but additional progestogen is required in the presence of a uterus.

- Progestogen therapy (progesterone and synthetic progestogens) is an option to treat hot flashes, but not as effective as estrogen
  - Long-term safety data are limited.
  - Primary use in postmenopausal women is to reduce risk of endometrial cancer associated with unopposed estrogen therapy (ET).

Hormone Therapy Management

- The risk of breast cancer in women over 50 years associated with MHT is a complex issue.
  - The increased risk of breast cancer is primarily associated with the addition of a progestogen to estrogen therapy and related to the duration of use.
    - An increased risk of breast cancer was seen with 3 to 5 years of estrogen-progesterone therapy use in WHI.
    - No increased risk of breast cancer was seen with 7 years of ET use, allowing for more flexibility in duration of ET use in women without a uterus.
  - The risk of breast cancer attributable to HT is small and the risk decreases after treatment is stopped.
  - Current safety data do not support the use of systemic HT in breast cancer survivors.
  - Low dose local vaginal estrogen therapy with minimal absorption appears to have minimal risk of recurrent breast cancer but decisions to use it in women with prior breast cancer should involve oncologist.

Hormone Therapy Management

- Overall in the literature, risk of DVT with oral HT appears increased at both younger and older ages and is supported in the WHI trial. Major concern with DVT is risk of PE, which was significantly increased in the WHI EPT trial.

- Overall data concerning risk of stroke with HT are mixed
  - Risk of stroke in WHI was increased but rare with both oral ET and EPT therapy
  - Not seen in other trials such as DOPS and WEST.

- The attributable risk of stroke due to HT for women who initiate HT under age 60 and/or within 10 years of menopause is rare.
**HT Duration of Use**

- HT should not be arbitrarily discontinued at age 65
  - In 42% of women aged 60-65, moderate to severe VMS have continued
  - VMS may persist for more than a decade
- Extending HT use is acceptable:
  - For women well aware of potential risks and benefits
  - With clinical supervision
  - With lowest effective dose
- For the woman
  - Who has determined the benefits of menopause symptom relief outweigh risks, notably after failing an attempt to stop hormone therapy
  - At high risk of osteoporosis-related fracture and bone loss for whom alternate therapies are inappropriate or cause unacceptable adverse effects

**NAMS expressed concerns about “BEERS Criteria” related to allowing “extended use of HT for women over 65 who are unable to discontinue HT”**

- Conceived in 1991, Clinical tool based on *The American Gerontological Society Criteria for Potentially Inappropriate Medication Use in Older Adults*
- Catalogues meds that cause adverse drug events in older adults due to their pharmacologic properties and the physiologic changes of aging.
- Purpose: Inform clinical decision-making concerning prescribing of meds for older adults in order to improve safety and quality of care.
- Used by NCQA as a quality measure in accreditation process of Insurance Companies.
- Not meant to be punitive.

**HT Routes of Administration**

- Systemic progestogen required for endometrial protection from unopposed systemic ET
- 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 treating solely vaginal symptoms; Progestogen generally not indicated with local, low-dose ET for vaginal atrophy.
HT Discontinuance

• 50% chance of vasomotor symptoms recur when HT discontinued
• Decision to continue HT must be individualized based on severity of symptoms and current benefit-risk ratio considerations
• Symptom recurrence similar whether tapered or abruptly discontinued.
  • In population-based multisite survey w 802 women, success more likely:
    • Had advice from provider on discontinuing
    • Had more favorable attitudes about menopause and HT discontinuation
    • Fewer symptoms upon discontinuation
    • Better symptom tolerance following discontinuation

HT & Vaginal Symptoms/Sexual Function

• ET most effective in treatment of moderate to severe urogenital atrophy and dyspareunia, common causes of intercourse avoidance
• Many systemic HT products and all local vaginal ET products have FDA approval for treating symptomatic vaginal atrophy
• HT not recommended as sole treatment of other sexual function problems independent from role in treating menopausal symptoms
  • Diminished sexual interest
  • Diminished arousal
  • Decreased orgasmic response

ANDROGENS

Key Points

• Androgen levels decline in women with aging but do not change across the menopause transition. Androgen levels are significantly lower in women with primary ovarian insufficiency and following bilateral oophorectomy.
• Evidence available to support use of testosterone therapy in carefully selected postmenopausal women with female sexual interest/arousal disorder (previously known as hypoactive sexual desire disorder) and no other identified etiology for their sexual problem.
• Long-term risks of androgen therapy in women, including possible effects on the risk of cardiovascular disease or breast cancer, are unknown.
• There are currently no androgen-containing prescription products FDA approved.
Androgens

Recommendations for Clinical Care

- A trial of testosterone therapy may be considered in carefully selected postmenopausal women with female sexual interest/arousal disorder and no other etiology for their sexual problems.
  - Women must be informed of potential adverse effects and unknown long-term risks. (Level I)
- No therapies approved by FDA for treating female sexual dysfunction D/T limited clinical trial data, limited efficacy compared with placebo, or concerns about long-term safety.
  - Women using testosterone should be monitored for adverse effects:
    - Facial hair, Acne, Voice changes, Clitoromegaly
    - Adverse changes in lipids or liver function tests.
- Blood testosterone levels should be checked intermittently to ensure that levels remain in the normal range for reproductive-aged women. Levels do not predict sexual function. (Level II)
  - There is currently no role for the use of DHEA in the treatment of female sexual disorders. (Level I)

Androgens

- Dosing: 300 mcg/day for six months was found to be safe and effective in women who were receiving concomitant estrogen therapy.
- One large trial reported similar results in menopausal women not taking estrogen/progestin therapy.
  - Most convenient formulation:
    - Topical compounded 1% cream or gel (0.5 grams daily) applied daily to the skin of arms, legs, or abdomen (last 10 days).
    - Very difficult to do accurately with available gels dosed for men in pumps and packets
    - FDA issued warning re reports of adverse effects on secondary exposure to children from adults
  - Benefits reported for many aspects of sexuality: desire, responsiveness, orgasm, & satisfaction

SERMS/TSEC

Key Points

- Compounds acting as estrogen agonists in some tissues and as estrogen antagonists in others. Different SERMs provide different tissue-specific actions, allowing for individualization depending on medical needs of the postmenopausal women.
- Available in US & Canada:
  - Tamoxifen, approved for prevention and treatment of breast cancer
  - Toremifene, approved for treatment of breast cancer
  - Raloxifene, approved for prevention and treatment of osteoporosis, and prevention of breast cancer. Increases risk of VTEs but does not increase the risk of uterine cancer.
- Bazedoxifene, approved for treatment of dyspareunia due to postmenopausal vaginal atrophy. No trials have evaluated bazedoxifene’s effects on the prevention or treatment of breast cancer or osteoporosis.
- TSEC: first tissue-selective estrogen complex - a pairing of conjugated estrogens with the SERM bazedoxifene, approved for the treatment of vasomotor symptoms & prevention of osteoporosis in women with a uterus. Bazedoxifene provides endometrial protection, so a progestrogen is not needed.

Recommendations for Clinical Care

- SERMs may be used to prevent breast cancer (tamoxifen, raloxifene), treat breast cancer (tamoxifen, toremifene), prevent and treat osteoporosis (raloxifene), and treat moderate to severe dyspareunia due to vaginal atrophy (bazedoxifene). (Level I)
- The TSEC bazedoxifene combined with conjugated estrogens may be used in women with a uterus to treat moderate to severe vasomotor symptoms and prevent osteoporosis. (Level I)
- SERMs should not be used in women at high risk of thrombosis because they increase the risk of VTEs, similar to oral estrogen therapy. (Level I)
Bio-Identical Hormone Therapy

Bio-Identical Hormones
- Many well-tested brand-name products containing “BHT” are approved in US/Canada.
- This term typically used to mean custom-made HT formulations compounded for an individual.
- Although the term *bioidentical hormones* is often used to describe custom-compounded HT products as they typically contain only hormones structurally identical to those produced by a woman’s ovaries during the reproductive years, the term was invented by marketers and has no clear scientific meaning.

Compounded Bio-Identical Hormones
- Compounding pharmacies are regulated by state pharmacy boards, with little oversight by FDA.
- Custom compounded BHT may provide doses, ingredients, and routes of administration not commercially available, but no formulation has been approved by any regulatory agency.
- BHT not tested for efficacy, safety, batch standardization, purity.
  - Compounded hormones do not routinely include the product information sheet required by FDA of commercially manufactured HT products.
  - Advertising and promotional claims regarding the efficacy and safety of compounded hormones are not validated by medical evidence.
  - Consumers generally are unaware of the limited control FDA exercises over the marketing and safety monitoring of compounded hormones.
- Salivary hormone testing (used to adjust custom BHT levels) has not been proven accurate or reliable.
Disclaimer!
Product Descriptions:
This discussion is not to be construed in any way as an endorsement of these products, nor are the products all inclusive of options.

www.menopause.org

HT/ET Prescription Options:
Oral

drospirenone and estradiol Tablets 0.5 mg/1 mg

Synthetic Conjugated Estrogens, B

HT/ET Prescription Options:
Progesterone

Generic Micronized Progesterone

Contraindication: Allergy to Peanut
HT/ET Prescription Options:

**Transdermals**

- New York Times article and blog: "When Hormone Creams Expose Others to Risks". When proper precautions aren't used with topical hormone products, both pets and family members are at risk for hormone exposure.
- Cases of transfer of topical estrogen preparations to pets and children have been reported with Evamist®. NAMS alerts women that transfer of estrogen to pets and children could occur with other estrogen skin products besides Evamist®.

**Vaginal**

- Conjugated estrogens vaginal cream: (0.625mg/g)
  - 1 gram intravaginally daily for 2 weeks, followed by 0.5 g intravaginally twice a week, for example, Monday and Thursday.

**Non-Oral Regimens**

- Transdermal (patch, cream, gel, or spray)
  - New York Times article and blog: "When Hormone Creams Expose Others to Risks". When proper precautions aren't used with topical hormone products, both pets and family members are at risk for hormone exposure.
  - Cases of transfer of topical estrogen preparations to pets and children have been reported with Evamist®. NAMS alerts women that transfer of estrogen to pets and children could occur with other estrogen skin products besides Evamist®.
Treatment of Dyspareunia

- Ospemifene (Osphena) 60mg daily
  - The only oral med and SERM approved in the US for the treatment of moderate to severe dyspareunia (FDA approved: 2013)
  - 12 weeks showed improvement in vaginal pH and vaginal dryness
    - No proliferative effect on endometrial tissue, no increase in thromboembolic events (Bachman & Komi, 2010)
    - Burich et al., (2012) - found to treat and prevent breast cancer in estrogen positive breast cancer cells in transgenic mouse model
    - Contraindicated in undiagnosed genital bleeding, estrogen dependent neoplasm, DVT, PE, or hx of these, stroke, MI, pregnancy

Water-based vaginal lubricants and Moisturizers

(Few clinical studies have been conducted on the efficacy of these products.)

"Replens, viable alternative to relieve vaginal dryness, vaginal fluid volume, improve pH, vaginal elasticity, reduce dyspareunia" (Bygdeman & Swan, 1996)

HT/ET Prescription Options: Vaginal Moisturizers

Non-Hormonal Options for Managing Vasomotor Flushes

- Additional Therapies (Off-Label):
  - Clonidine (Transdermal) is a centrally acting used in the treatment of HTN.
  - Studied more extensively in 1970s-1990s with mixed results in reduction of hot flashes
  - Recent trial using clonidine for patients on tamoxifen therapy showed a 38% reduction in hot flushes per day (Pandya et al., 2000)
  - Modest effect on symptoms, adverse side effects (insomnia, dry mouth, constipation, drowsiness.) May be a good choice for patients with HTN
Non-Hormonal Options for Managing Vasomotor Flushes

- FDA Approved 2013
  - Paroxetine (Brisdelle) 7.5 mg one capsule taken at bedtime
  - Contains a lower dose of paroxetine than that used for psychiatric conditions
- Off-Label Management of Symptoms:
  - Venlafaxine (Effexor XR) 37.5 mg a day- titrate as needed; commonly 75 mg/day
  - Desvenlafaxine (Pristiq) 50-100 mg/day
    - Studied extensively following US FDA guidance trials in postmenopausal women with moderate to severe hot flashes
    - Total of four randomized, placebo controlled trials found significant reduction of hot flashes at 100mg QD (Speroff et al., 2008; Archer et al., 2009; Archer et al., 2009; Pickar et al., 2007).
  - Some SSRIs and SNRIs inhibit the cytochrome P450 enzyme system and may render tamoxifen less effective.
  - Women using tamoxifen for the prevention or treatment of breast cancer should avoid the use of paroxetine for management of vasomotor symptoms.(Level III)
- Venlafaxine (Effexor XR) 75 mg/day
- Desvenlafaxine (Pristiq) 50-100 mg/day

Non-Hormonal Options for Managing Vasomotor Flushes

- Additional Therapies (Off Label):
  - Gabapentin (Neurontin)-indicated in treatment of partial seizures and post herpetic neuralgia; studied in hot flash reduction
    - Pandya et al., (2005) studied with breast cancer patients (n=420) and found hot flush frequency was reduced by 44% at 900mg/day.
  - “Gralise” : titrated to an 1800 mg daily dose, taken orally, 600 mg with the morning meal and 1200 mg with the evening meal.
  - Adverse effects include dizziness, somnolence, peripheral edema

Alternatives for Managing Vasomotor Flushes

- Yoga
- Acupuncture
- Exercise

Thurston et al., 2006 (n= 523) found for women with concomitant depression, physical activity was associated with decreased risk for vasomotor symptoms
Exercise may be associated with shorter duration of hot flashes
Alternatives for Managing Vasomotor Flushes:

- **Black Cohosh**
  - Study results are mixed on whether Black Cohosh effectively relieves menopausal symptoms. An NCCAM-funded study found that black cohosh, whether used alone or w other botanicals, compared to placebo failed to relieve vasomotor flushes & night sweats in PMW or those approaching menopause. In general, clinical trials of black cohosh for menopausal symptoms have not found serious side effects.

- **Isoflavones/Soy**
  - Modestly effective in relieving symptoms
  - More clinical studies are needed to compare outcomes among women who have ability to convert daidzein to equol with those that lack that ability. Do equol producers derive greater benefits from soy supplementation?

NAMS Menopause Decision Support App

MenoPro

- Free downloadable mobile app for clinicians or women
- Purpose: Choose the optimal treatment by individualizing treatment based on personal preferences and risk factors
- Users progress through a series of questions to:
  - Assess symptom severity
  - Calculate CV risks
  - Evaluate risk for reproductive organ cancer
- Users obtain evidence-based information about risks and benefits of each treatment option
  - Lifestyle modifications
  - Non-prescription therapies
  - Hormone therapies
  - Prescription non-hormone therapies
- If available by Wi-Fi accessibility, users or women can print out choices for further discussion.

Options with the App

- Treatment for moderate to severe hot flashes and/or night sweats
- Symptoms of vaginal dryness, pain with sexual activity or urinary issues (GSM)
- Convenient links to information about treatment choices, formulations and doses and “contraindications”
- Calculations of CVD risk score over next 10 years
- Links to GAIL model to calculate risk of breast cancer risk
- Link to FRAX to determine risk of osteoporosis.
Decision-Making Process and Treatment Options

- Key elements include
  - Assessment of presence of bothersome symptoms
  - Personal preference regarding hormone versus non-hormone treatments
  - Presence of risk factors that might make woman ineligible for treatment
  - Assessment of years since menopause and baseline risks of CVD, breast cancer, and other health problems
  - Review of benefits and risks of treatment
- If HT is chosen makes suggestion of transdermal vs for patients with metabolic syndrome or other significant CVD risk.
- A similar process is followed for non-hormone treatment for women who are not candidates for, or who choose not to take HT suggesting Paroxetine or other antidepressants or different medications options.
- Recommendations for vaginal meds are given.
- A section is available for women to use in the “Self-Assessment Section” to share a summary with their provider, and review comments and definition at the end of that section.
Minnie Pauz.....

"Bright, cheerful single girl..." noooh...
"Mature, independent female..." nope...
Oh well... "1940 model, chassis needs work, but engine still hums under the hood!"