Dr. Malieri Colon-Rivera, originally from Carolina, Puerto Rico moved to Trinity in July 2014. She joined Dr. Wanda Torres at Suncoast Women’s Care.

Joining a practice for women by women, her mission is to provide patient care according to medical guidelines with the highest ethical principles and gentle care.

Dr Colon-Rivera demonstrates her commitment and dedication to her medical education having been awarded by her peers during her residency.

Dr. Colon-Rivera is member of the American College of Obstetrics and Gynecologist.

Dr. Colon-Rivera is continually striving to improve the well being of her patients and offers minimally invasive surgical procedures. Dr. Colon-Rivera has hospital privileges at Mease Countryside Hospital and Morton Plant North Bay Hospital.
Introduction to Menopause

- The time in a woman's life
- Usually between age 45 and 55 years, it is completed after cessation of menstrual periods for 12 months. The average age is 51 years. (up to date)
- Most women experience several years of changes in their menstrual periods before menopause.
- Menopause is a normal part of a woman's life and does not always need to be treated. However, the changes that happen before and after menopause can be disruptive. If you have bothersome symptoms, effective treatments are available. (up to date)
Stages of Change

The menopausal transition "perimenopause" is the time when your periods start to change and ends with your final menstrual period (FMP). Usually 4 years in average.

- Less frequent periods? Ex: Every 6 weeks instead of every 4 weeks.
- Lasting less days? Ex: 3 days instead of 5.
- Bleeding less? Using less pads a day.
- Skipping periods?
- Having “menopausal” symptoms?

Menopause LMP-12th month without menstrual periods

"Postmenopause" is the time after menopause (a woman who has been through menopause can be described as “postmenopausal”).
Stages of Change

- Much of the available information about the endocrine and clinical manifestations of the menopausal transition comes from a number of longitudinal cohort studies of midlife women [7], the largest of which, is the Study of Women’s Health Across the Nation (SWAN), has followed a multiethnic, community-based cohort of over 3,000 women from ages 42 to 52 years for 15 years [7,12-14,16,17,20-29].
Menopause is a reflection of complete, or near complete, ovarian follicular depletion, with resulting hypoestrogenemia and high follicle-stimulating hormone (FSH) concentrations.

A comparison of the relationship between age and primordial follicle number in Block’s study of 44 girls and women aged 7 to 44 years with that of Gougeon’s study of women aged 45 to 55 years. Follicle depletion appears to accelerate in the decade preceding menopause.

Data from:
But what if I already have a hysterectomy? How do I Know?

- After hysterectomy —if you still have ovaries, you will still go through menopause when your ovaries stop ovulating and the production of estrogen diminishes. Usually the key to identify menopause in these patients is:
  a. Age: (45-55) year old
  b. The presence of “menopausal symptoms”
  c. These symptoms are not relieved by correcting thyroid dysfunction if any.
Premature Ovarian Failure

Early Menopause (40-44) year old

POF:
1. 39 years old or less
2. Bilateral Salpingophorectomy (BSO)
4. Tx: 17 beta estradiol 0.1 mg transdermal (preferred, when there is no contraindication of comorbidities)
5. Karyotype?
What if I bleed after Menopause?

Postmenopausal Bleeding

- Approximately 4 to 11 percent of postmenopausal women.

- Where is the bleeding coming from?
  a) Intrauterine
  b) cervix, vagina, vulva,
  c) fallopian tubes
  d) related to ovarian pathology.
  e) The origin of bleeding can also involve nongynecologic sites, such as the urethra, bladder, and rectum/bowel.
Causes of Postmenopausal (uterine) Bleeding:

1. **Endometrial Atrophy** — atrophic endometrial surfaces contain little microerosions causing a subsequent chronic inflammatory reaction (chronic endometritis), which is prone to light bleeding or spotting.

2. **Cancer** — Approximately 5 to 10 percent of women with postmenopausal vaginal bleeding have endometrial cancer.
   - Adenocarcinoma of the endometrium is the most common genital cancer in women over 45 years of age.
   - Sarcomas of the uterus constitute only 3 to 5 percent of all uterine tumors and may present with postmenopausal bleeding.
   - Fallopian tube or ovarian cancer can cause postmenopausal uterine bleeding. Cervical and vaginal cancers typically present with vaginal bleeding. Vulvar cancers are not associated with bleeding until they are advanced. (See individual topic reviews for each cancer).

3. **Polyps** — Polyps are benign endometrial growths of unknown etiology that are a common cause of perimenopausal and early postmenopausal uterine bleeding.

4. **Postmenopausal hormone therapy** — many postmenopausal women who take estrogen therapy develop vaginal bleeding; (intermittent progesterone regimen).

5. **Endometrial hyperplasia** — endometrial hyperplasia may manifest clinically as uterine bleeding.
Causes of Postmenopausal bleeding:

6. **Leiomyomata uteri** — The prevalence in postmenopausal women is 1/10 that of premenopausal women, thus they are a potential, but uncommon, cause of uterine bleeding in menopausal women.

7. **Disease in adjacent organs** — Inflammation of neighboring organs, Examples: a ruptured sigmoid diverticulum may fistulize into the uterus and present as uterine bleeding, bleeding hemorrhoids, Bladder Cancer may cause bleeding that is mistaken for genital tract bleeding.

8. **Post radiation therapy** — Vaginal bleeding can be a late effect of radiation therapy.

8. **Anticoagulant therapy**

9. **Herbal and dietary supplements** — Soy and other phytoestrogens in large doses may be associated with stimulation of the endometrial lining. One series reports the association of soy with polyp and leiomyoma growth.

10. **Infection** — Endometritis.

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Evaluation of Postmenopausal Bleeding
Steps in evaluation of Postmenopausal Bleeding
Steps in evaluation of Postmenopausal Bleeding
Endometrial Biopsy for Postmenopausal Bleeding
Hysteroscopy, D and C, Polypectomy
The Most Common Menopause Symptoms

- Hot Flashes
- Night Sweats
- Irregular Periods
- Loss of Libido
- Vaginal Dryness
Menopausal Symptoms

1. **Hot flashes** – Hot flashes are

   – The most common - 60 to 80% of women.

   – Sudden feeling of heat in the upper chest and face then spreads throughout the body and lasts for at least 2 minutes.

   – Sweat, chills, anxiety, palpitations may be present.

   – (1/day-1/hour)
Menopausal Symptoms

2. **Night sweats** – Hot flashes that are more common at night. Complications: decrease concentration, fatigue, irritability, mood swings, decrease or absent libido.

3. **Sleep problems** – Trouble falling asleep or staying asleep.
Menopausal Symptoms

4. **Vaginal dryness** – As the levels of estrogen in the body decreases this tissue become thin and dry. Complains of discomfort with touch or clothing, itching, or pain during sex and decrease libido.
Figure 2

The Vaginal Epithelium

- Superficial cells
- Intermediate cells
- Parabasal cells
- Basal cells
5. **Depression** – During the menopausal transition, many women develop new problems with mood, such as sadness, difficulty concentrating, feeling uninterested in normal activities, and sleeping too much or having trouble staying asleep. Women with a past history of depression may notice a recurrence during the menopause transition. If you have any symptoms of depression or blues that will not go away, talk to your doctor or nurse. (up to date)
6. **Sexual function** — Estrogen deficiency leads to a decrease in blood flow to the vagina and vulva causing decreased vaginal lubrication, vaginal dryness, dyspareunia. The vagina becomes thin, the elasticity of the vaginal wall may decrease and the entire vagina can become shorter or narrower. The cervix also can atrophy and become flush to the vagina.
Vulvar and Vaginal Atrophy
Vaginal estrogen preparations available in the United States for treatment of vaginal atrophy

<table>
<thead>
<tr>
<th>Preparation (United States trade name)</th>
<th>Available strengths</th>
<th>Regimen (FDA-approved prescribing information)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal ring</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrin</td>
<td>7.5 mcg estradiol/day, released over 90 days</td>
<td>Ring is inserted into the vagina by the patient or clinician. Ring is removed and replaced with a new ring every 90 days.</td>
</tr>
<tr>
<td><strong>Vaginal tablet</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vagifem</td>
<td>10 mcg estradiol per vaginal tablet</td>
<td>Insert 1 tablet intravaginally daily for 2 weeks, followed by twice weekly.</td>
</tr>
<tr>
<td><strong>Vaginal cream</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premarin</td>
<td>0.625 mg conjugated estrogens per gram of cream</td>
<td>0.5 gram of cream intravaginally administered twice weekly. Cyclic regimen also listed in approved product information, but not commonly used.</td>
</tr>
<tr>
<td>Estrace</td>
<td>100 mcg estradiol per gram of cream</td>
<td>0.5 grams of cream intravaginally administered daily for one or two weeks, then reduce to twice weekly.</td>
</tr>
</tbody>
</table>

FDA: US Food and Drug Administration.

Menopausal Symptoms

7. Breast pain
8. Headache - Migraine, Clusters

Both are more common in perimenopause.
Long Term Effects of Estrogen Deficiency

- **Bone loss**

- **Joint pain** — Joint aches and pain are a commonly reported symptom among women at midlife. The Women's Health Initiative, women with joint pain were more likely to get relief with either combined estrogen-progestin therapy or unopposed estrogen than with placebo.

- **Degenerative arthritis** — Estrogen deficiency after menopause may contribute to the development of osteoarthritis, but data are limited.

- **Body composition** — In the early postmenopausal years, women who do not take estrogen therapy typically gain fat mass and loose lean mass.
Menopausal Symptoms

- Impaired cognitive function-
estrogen has an important role on
cognitive function, depression, and
sleep disturbances has an additive
effect.

As you get older
three things
happen.
The first is
your memory
goes, and
I can't remember
the other two.
- Sir Norman Wisdom
The Stages of Reproductive Aging Workshop +10 staging system for reproductive aging in women

<table>
<thead>
<tr>
<th>Stage</th>
<th>-5</th>
<th>-4</th>
<th>-3b</th>
<th>-3a</th>
<th>-2</th>
<th>-1</th>
<th>+1a</th>
<th>+1b</th>
<th>+1c</th>
<th>+2</th>
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</thead>
<tbody>
<tr>
<td>Terminology</td>
<td>REPRODUCTIVE</td>
<td>MENOPAUSAL TRANSITION</td>
<td>POSTMENOPAUSE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>Variable</td>
<td>Variable</td>
<td>1-3 years</td>
<td>2 years (1+1)</td>
<td>3-6 years</td>
<td>Remaining lifespan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PRINCIPAL CRITERIA**

| Menstrual cycle | Variable to regular | Regular | Regular | Subtle changes in flow/strength | Variable length: Persistent >7-day difference in length of consecutive cycles | Interval of amenorrhea of >=60 days |

**SUPPORTIVE CRITERIA**

<table>
<thead>
<tr>
<th>Endocrine</th>
<th>FSH</th>
<th>AMH</th>
<th>Inhibin B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Low</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antral follicle count</th>
<th>Low</th>
<th>Low</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasomotor symptoms Likely</td>
</tr>
<tr>
<td>Vasomotor symptoms Most likely</td>
</tr>
<tr>
<td>Increasing symptoms of urogenital atrophy</td>
</tr>
</tbody>
</table>

Arrow: elevated; FMP: final menstrual period; FSH: follicle-stimulating hormone; AMH: anti-mullerian hormone.
* Blood draw on cycle days 2 to 5.
• Approximate expected level based on assays using current international pituitary standard.

Menopause Hormone Therapy (MHT)

OCP’s:
- Non Smokers, until 51 y/o, still having irregular menstrual periods. MHT and contraception.
- 2-3% of pregnancy in this population
- Menopausal patients- Tapering off 1 pill per week to decrease chances of sudden vasomotor symptoms.
- Uncertain if menopausal- discontinue OCP, measure FSH on wk #4. (FSH: 25 or more correlates with perimenopausal transition, FSH: 70 or more correlates with menopausal values)

After 52 y/o, known menopausal:
Conjugated Estrogen 0.625 mg/day (orally)
17-beta estradiol 1 mg/d (orally)
17-beta estradiol 0.5 mg/d (transdermal)
-Stop hot flashes in 80% of patients, HF are decreased in 20% of the remaining patients.
Start transdermal 0.025 mg/patch or oral estradiol 0.5 mg/day, and titrate up to relieve symptoms.

Transdermal 0.0375 mg/patch or oral estradiol 1 mg/day

Transdermal 0.05 mg patch or oral estradiol 2 mg/day
Medroxyprogesterone acetate (MPA) is the most studied.
- Recommended dose 2.5 mg orally /daily

Alternative to MPA is the natural micronized progesterone:
- First Year after menopause: 200mg/day x 12 days each month (associated to mood changes, bloating, breakthrough spotting bleeding) (cyclic)
- 2nd and 3rd year of menopause: 100 mg daily (continuous)

Poor tolerance to progesterone: mood swings, bloating, breast tenderness.
- Off label Mirena IUD use:
- Bazedoxifene (SERN): FDA approved for treatment of hot flashes and osteoporosis prevention.

Progestin's

 ✓ Short therapy (2-3 years)
 ✓ Regular Therapy (5 years)

WHI: EPT increase risk of primary invasive breast ca in year of therapy #4.
Contraindications to MHT

1. Personal history of breast cancer
2. Chronic Liver Disease
3. Previous Venous Thromboembolic Disease
4. Active Liver Disease
Special Circumstances:

1. Patient with **migraines** and **HF**: respond better to transdermal approach, also options of non hormonal treatment.
2. **Depressive** patients: hot flashes respond better to estrogen, depression to SSRI’s.
3. **Vulvar atrophy**: respond better to local, vaginal estrogen.
   - Can use vaginal moisturizers twice a week if vaginal estrogen is contraindicated.
   - Ospemiphene (SERN)
Special Circumstances

**Ospemifene** is effective in treating dyspareunia and vaginal dryness in menopausal women with vulvovaginal atrophy. No studies to-date have compared with vaginal estrogen therapy.

Ospemifene (60 mg orally, 12 weeks of therapy) was more effective than placebo in improving dyspareunia, although the benefit beyond that of placebo was modest but significantly decrease vaginal dryness.

- Hot flushes were the most common adverse effect.
- Benefit: Appears to have a favorable endometrial safety profile.
- Potential risk: Thrombotic adverse effects are a potential risk with SERMs. There have been no reports.

- Animal and preclinical data suggest that ospemifene has a neutral or inhibitory effect on carcinogenesis in the breast [c,d]. Further study is needed to evaluate the safety of Ospemifene in women with breast cancer, or whether it may have a protective effect for women at high risk for breast malignancy.

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## Vaginal moisturizers and lubricants

<table>
<thead>
<tr>
<th>Product (manufacturer)</th>
<th>Ingredients</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Moisturizers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rephans®</td>
<td>Water, carboxyl, polyacryl, paraffin, hydrogenated palm oil, glycerol, sorbic acid, and sodium hydroxide</td>
<td>Should be used 3 times weekly</td>
</tr>
<tr>
<td>Me Again™</td>
<td>Water, carboxyl, aloe, citric acid, chlorhexidine degradate, sodium benzoate, potassium sorbate, disodium sodium, and sorbic acid</td>
<td></td>
</tr>
<tr>
<td>Vagisil® Feminine Moisturizer</td>
<td>Water, glycerin, propylene glycol, poloxamer 407, methylparaben, polyquaternium-32, propylene glycol, chamomile, and aloe</td>
<td></td>
</tr>
<tr>
<td>Femihaze®</td>
<td>Water, mineral oil, glycerin, yarba santa, caprylic alcohol, and methyl paraben</td>
<td>Yarba santa (Eriocaulon spp.), a plant native to the Pacific Northwest, is used as a moisturizer in place of aloe</td>
</tr>
<tr>
<td>K-Y® SILK-E®</td>
<td>Water, propylene glycol, sorbitol, polysorbate 80, hydroxyethylcellulose, benzoic acid, methylparaben, tocopherol, and aloe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Lubricants</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water-based</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slippery Stuff®</td>
<td>Water, polyoxyethylene, methylparaben, propylene glycol, isopropyl</td>
<td></td>
</tr>
<tr>
<td>Astroglide®</td>
<td>Water, glycerin, methylparaben, propylene glycol, polypropylene glycol, polyquaternium, hydroxyethylcellulose, and sodium benzoate</td>
<td>Also sold in a glycerin-free and paraben-free formulation</td>
</tr>
<tr>
<td>K-Y® Jelly</td>
<td>Water, glycerin, hydroxyethylcellulose, parabens, and chlorhexidine</td>
<td></td>
</tr>
<tr>
<td>Pre-Seed®</td>
<td>Water, hydroxyethylcellulose, arabinogalactan, paraben, and Pluronic copolymers</td>
<td>Promoted to women and their partners who are trying to conceive</td>
</tr>
</tbody>
</table>

| **Silicone-based**      |             |       |
| ID® Millennium          | Cyclomethicone, dimethicone, and dimethiconol | Less drying than other lubricants |
| Pjur® Eros              | Cyclopentasiloxane, dimethicone, and dimethiconol | Compatible with a condom |
| Pink™                   | Dimethicone, vitamin E, aloe vera, dimethiconol, and cyclomethicone | Compatible with a condom |

| **Oil-based**           |             |       |
| Elegance Women’s Lubricant | Natural oils | Does not contain alcohol, glycerin, or parabens; is not compatible with a condom |

### Vaginal estrogen preparations available in the United States for treatment of vaginal atrophy

<table>
<thead>
<tr>
<th>Preparation (United States trade name)</th>
<th>Available strengths</th>
<th>Regimen (FDA-approved prescribing information)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal ring</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td>7.5 mcg estradiol/day, released over 90 days</td>
<td>Ring is inserted into the vagina by the patient or clinician. Ring is removed and replaced with a new ring every 90 days.</td>
</tr>
<tr>
<td><strong>Vaginal tablet</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vagifem</td>
<td>10 mcg estradiol per vaginal tablet</td>
<td>Insert 1 tablet intravaginally daily for 2 weeks, followed by twice weekly.</td>
</tr>
<tr>
<td><strong>Vaginal cream</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premarin</td>
<td>0.625 mg conjugated estrogens per gram of cream</td>
<td>0.5 gram of cream intravaginally administered twice weekly. Cyclic regimen also listed in approved product information, but not commonly used.</td>
</tr>
<tr>
<td>Estrace</td>
<td>100 mcg estradiol per gram of cream</td>
<td>0.5 grams of cream intravaginally administered daily for one or two weeks, then reduce to twice weekly.</td>
</tr>
</tbody>
</table>

FDA: US Food and Drug Administration.

Table X. Estrogen therapy products approved for postmenopausal use in the United States

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product name(s)</th>
<th>Range of available dose strengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogens</td>
<td>Premarin</td>
<td>0.3-1.25 mg</td>
</tr>
<tr>
<td>Synthetic conjugated estrogens, A*</td>
<td>Cenestin</td>
<td>0.3-1.25 mg</td>
</tr>
<tr>
<td>Synthetic conjugated estrogens, B**</td>
<td>Enjuvia</td>
<td>0.3-1.25 mg</td>
</tr>
<tr>
<td>Esterified estrogens</td>
<td>Menest</td>
<td>0.3-1.25 mg</td>
</tr>
<tr>
<td>17β-estradiol</td>
<td>Estrace, various generics</td>
<td>0.5-2.0 mg</td>
</tr>
<tr>
<td>Estradiol acetate</td>
<td>Femtrace</td>
<td>0.45-1.8 mg</td>
</tr>
<tr>
<td>Estropipate</td>
<td>Ortho-Est</td>
<td>0.625 mg (0.75 mg estropipate, calculated as sodium estrone sulfate 0.625 mg) to 5.0 mg (6.0 mg)</td>
</tr>
</tbody>
</table>

** Transdermal products **

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product name(s)</th>
<th>Dose details</th>
</tr>
</thead>
<tbody>
<tr>
<td>17β-estradiol matrix patch</td>
<td>Alora, Climara, Esclim, Fempatch, Menostar, Vivelle, Vivelle-Dot, various generics</td>
<td>0.014-0.1 mg delivered daily; applied once or twice weekly</td>
</tr>
<tr>
<td>17β-estradiol reservoir patch</td>
<td>Estraderm</td>
<td>0.05-0.1 mg delivered daily; applied twice weekly</td>
</tr>
<tr>
<td>17β-estradiol transdermal gel</td>
<td>EstroGel, Elestrin, Divigel</td>
<td>Applied daily via metered pump or packet delivering 0.52-0.75 mg of 17β-estradiol in gel</td>
</tr>
<tr>
<td>17β-estradiol topical emulsion</td>
<td>Estrasorb</td>
<td>2 packets applied daily</td>
</tr>
<tr>
<td>17β-estradiol transdermal spray</td>
<td>Evamist</td>
<td>1 spray/d, up to 2-3/d if needed</td>
</tr>
</tbody>
</table>

* 9 estrogens
** 10 estrogens
<table>
<thead>
<tr>
<th>Composition</th>
<th>Product name(s)</th>
<th>Dose details</th>
</tr>
</thead>
<tbody>
<tr>
<td>17β-estradiol vaginal cream*</td>
<td>Estrace Vaginal Cream</td>
<td>Initially 2-4 g/d for 1-2 wk, followed by maintenance dose of 1 g/d (0.1 mg active ingredient/g)</td>
</tr>
<tr>
<td>Conjugated estrogens cream*</td>
<td>Premarin Vaginal Cream</td>
<td>For vaginal atrophy: 0.5-2 g/d for 21 d then off 7 d  For dyspareunia: 0.5 g/d for 21 d then off 7 d, or twice weekly (0.625 mg active ingredient/g)</td>
</tr>
<tr>
<td>17β-estradiol vaginal ring</td>
<td>Estring</td>
<td>Device containing 2 mg releases 7.5 μg/d for 90 days (for vulvovaginal atrophy)</td>
</tr>
<tr>
<td>Estradiol acetate vaginal ring</td>
<td>Femring</td>
<td>Device containing 12.4 mg or 24.8 mg estradiol acetate releases 0.05 mg/d or 0.10 mg/d estradiol for 90 days (both doses release systemic levels for treatment of vulvovaginal atrophy and vasomotor symptoms)</td>
</tr>
<tr>
<td>Estradiol hemihydrate vaginal tablet</td>
<td>Vagifem</td>
<td>Initially 1 tablet/d for 2 wk, followed by 1 tablet twice weekly (tablet 10 μg of estradiol hemihydrates, equivalent to 10 μg of estradiol; for vulvovaginal atrophy)</td>
</tr>
</tbody>
</table>

*N.B. Higher doses of vaginal estrogen are systemic, meant to relieve hot flashes as well as vaginal atrophy; the lower doses are intended for vaginal symptoms only even though a small amount does get absorbed.
<table>
<thead>
<tr>
<th>Product name(s)</th>
<th>Standard/low dose</th>
<th>Estrogen</th>
<th>Progestogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prempro</td>
<td>Standard</td>
<td>0.625 mg conjugated estrogens</td>
<td>2.5 or 5 mg medroxyprogesterone acetate</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>0.3 or 0.45 conjugated estrogens</td>
<td>1.5 mg medroxyprogesterone acetate</td>
</tr>
<tr>
<td>Femhrt</td>
<td>Standard</td>
<td>5 µg ethinyl estradiol</td>
<td>1 mg norethindrone acetate</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>2.5 µg ethinyl estradiol</td>
<td>0.5 mg norethindrone acetate</td>
</tr>
<tr>
<td>Activella</td>
<td>Standard</td>
<td>1 mg 17β-estradiol</td>
<td>0.5 mg norethindrone acetate</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>0.5 mg 17β-estradiol</td>
<td>0.1 mg norethindrone acetate</td>
</tr>
<tr>
<td>Angeliq</td>
<td>Low</td>
<td>0.5 mg 17β-estradiol</td>
<td>1 mg drospirenone</td>
</tr>
<tr>
<td></td>
<td>Lower</td>
<td>0.25 mg 17β-estradiol</td>
<td>0.5 mg drospirenone</td>
</tr>
</tbody>
</table>
Updated summary of the effects of orally administered CEE alone or combined with MPA in women ages 50 to 59 years during intervention phase of WHI. One set of analyses examined the risks and benefits of these agents in women ages 50 to 59 years. This figure plots these data, which are expressed here as excess risks and benefits per 1000 women using MHT for five years. Because women deciding to use MHT are more likely to continue this for a period of years rather than one year, this figure is constructed according to that assumption. WHI studies were not powered for age-related subset analyses, and none of the data presented in the figure are statistically significant. Nonetheless, this figure represents the best estimates that are available at the present time and are likely more reliable than similar estimates based on observational studies as reported previously in The Endocrine Society Scientific Statement.

The HR (95% CI) values for the bars in the figure are listed here with reference to the alphabetical designations shown next to the bars: (a) HR 0.60 (0.35-1.04); (b) HR 1.34 (0.82-2.19); (c) HR 0.82 (0.50-1.34); (d) HR 1.21 (0.81-1.80); (e) HR 0.99 (0.53-1.85); (f) HR 1.51 (0.81-2.82); (g) HR 1.53 (0.63-3.75); (h) HR 2.05 (0.89-4.71); (i) HR 1.66 (0.76-3.67); (j) HR 3.01 (1.36-6.66); (k) HR 0.71 (0.30-1.67); (l) HR 0.70 (0.29-2.18); (m) HR 1.00 (ns-ns); (n) HR 1.12 (0.45-2.75); (o) HR 0.62 (0.30-1.29); (p) HR 0.90 (0.72-1.11); (q) HR 0.62 (0.68-1.00); (r) HR 5.01 (0.59-42.9); (s) HR 0.17 (0.02-1.45); (t) HR 0.70 (0.46-1.09); (u) HR 0.67 (0.43-1.04); (v) HR 0.83 (0.67-1.04); and (w) HR 0.85 (0.66-1.09). (RJ Santen, et al. Competency in menopause management: whither goest the internist? J Women's Health (Larchmt) 2014; 23:281, courtesy of Mary Ann Liebert, Inc.)

CEE: conjugated equine estrogen; E: estrogen; E+P: estrogen-progesterin; HR: hazard ratio; MHT: menopausal hormone therapy; MPA: medroxyprogesterone acetate; WHI: Women's Health Initiative.

## Risks and benefits of menopausal hormone therapy (MHT)

<table>
<thead>
<tr>
<th>Number of women per 1000 per 5 years of use</th>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
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<tr>
<td>Invasive breast cancer</td>
<td></td>
<td></td>
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<tr>
<td>StROKE</td>
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<tr>
<td>Pulmonary embolism</td>
<td></td>
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<tr>
<td>Deep vein thrombosis</td>
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<tr>
<td>Colorectal cancer</td>
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<tr>
<td>Endometrial cancer</td>
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<tr>
<td>Lung cancer</td>
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<tr>
<td>All fractures</td>
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<tr>
<td>Hip fractures</td>
<td></td>
<td></td>
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<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes</td>
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</tr>
</tbody>
</table>

### Risks

- Postmenopausal women (50–59 years of age)

#### Summary

Updated summary of the effects of orally administered CEE alone or combined with MPA in women ages 50 to 59 years during intervention phase of WHI. One set of analyses examined the risks and benefits of these agents in women ages 50 to 59 years. This figure plots the data, which are expressed here as excess risks and benefits per 1000 women using MHT for five years. Because women deciding to use MHT are more likely to continue this for a period of years rather than one year, this figure is constructed according to that assumption. WHI studies were not powered for age-related subset analyses, and none of the data presented in the figure are statistically significant. Nonetheless, this figure represents the best estimates that are available at the present time and are likely more reliable than similar estimates based on observational studies as reported previously in The Endocrine Society Scientific Statement.

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Women’s Health Initiative (WHI)

- **Women’s Health Initiative (WHI)** — In the past, MHT was also often prescribed for prevention of coronary heart disease (CHD) and osteoporosis, based upon epidemiologic data demonstrating a protective effect of estrogen on the heart and bone. However, data from the WHI, a set of two hormone therapy (HT) trials (unopposed estrogen and continuous, combined estrogen-progestin therapy versus placebo) in approximately 27,000 postmenopausal women (mean age 63 years) showed a number of adverse outcomes, including an excess risk of CHD, stroke, venous thromboembolism (VTE), and breast cancer 2002 (e,f,g).

- Most experts suggest that combined therapy be limited to five years of use (because of an increased risk of breast cancer). However, there may be more flexibility in duration of use with unopposed estrogen.

- While the WHI clearly demonstrated the adverse effects of HT in older postmenopausal women (over age 60 years), this is not the age group that presents with new onset of menopausal symptoms. Almost all women who seek medical therapy for menopausal symptoms do so in their late 40s or 50s.

- MHT, benefits for up to five years of treatment in young postmenopausal women (e.g., <10 years postmenopausal, or ages 50 to 59 years). Women should be reassured that the absolute risk of complications for healthy, young postmenopausal women taking HT for five years is very low.

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g. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women’s Health Initiative randomized trials. JAMA 2013; 310:1353.

UpToDate Menopausal hormone therapy: Benefits and risks. Kathryn A Martin, MD, Robert L Barbieri, MD et al.
Nonhormonal treatment for Menopausal Symptoms.

- Nonhormonal prescription drugs (off-label use):
  - Antidepressant
    - SSRIs: fluoxetine, paroxetine, escitalopram
    - SNRIs: venlafaxine and desvenlafaxine
  - Hypnotic
    - Eszopiclone
  - Anticonvulsant
    - Gabapentin
  - Antihypertensive
    - Clonidine
Nonhormonal treatment for Menopausal Symptoms.

- **Lifestyle changes**
  - Try relaxation techniques (eg, yoga, meditation)
  - Eat a healthy diet
  - Get regular exercise
  - Avoid hot flash triggers (eg, caffeine, alcohol, spicy food)
  - Keep cool
    - *Dress in layers (eg, light or wicking clothing)*
    - *Sleep in cool room (eg, fan, thermoregulation pillow)*
    - *Consume cold drinks*

- **Reduce sexual discomfort and increase sensitivity with moisturizers, lubricants, and vibrators**

- **Smoking cessation**
The following organizations and web sites also provide reliable health information:

- National Library of Medicine
- Hormone Health Network
  www.hormone.org/diseases-and-conditions/womens-health/menopause-map#/intro/
- North American Menopause Society
- Menopause.org
  www.menopause.org
- Vaginismus.com
  www.vaginismus.com