Don't Sweat It: **Consulting RxFiles in Menopause Management**

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VANCOUVER CONVENTION CENTRE

FMF
Family Medicine Forum
Forum en médecine familiale

THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
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Presenter Disclosure

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Relationships with financial sponsors:

- Any direct financial relationships, including receipt of honoraria:
  - RxFiles Academic Detailing Employee (University of Saskatchewan)
- Membership on advisory boards or speakers' bureaus: nil
- Patents for drugs or devices: nil
- Other: nil

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- Any direct financial relationships, including receipt of honoraria:
  - Consultant with RxFiles Academic Detailing
- Membership on advisory boards or speakers' bureaus: nil
- Patents for drugs or devices: nil
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Disclosure of Financial Support

- RxFiles Academic Detailing
  - Receives grants from SK Health through the University of Saskatchewan for academic detailing in SK.
  - Receives revenue from the sale of book & subscriptions, and from annual conference registrations; *not for profit- not for loss*.
- RxFiles **does not** receive funding from the pharmaceutical industry.
- Neither Taisa nor Debbie have received any external financial support.

Learning Objectives

- To improve clinician confidence in providing care for people in the menopause transition by addressing practical, case-based considerations, such as:
  a) Individualizing **menopause hormone therapy** (MHT) regimens.
  b) Addressing patient questions around symptoms and **treatment expectations during peri-menopause.**
  c) Taking a personalized approach when **treating genitourinary syndrome** of menopause.
  d) Using **non-hormonal options** for treating vasomotor symptoms.
  e) Navigating **challenging** scenarios / patient concerns where the **evidence is limited and evolving**.
  f) Utilizing **clinical tools for education and shared decision making**.

Gender Terminology

- Our resources are most relevant for people born with ovaries. To remain consistent with the research we reference, we will use the term “women;” however, we acknowledge that this term does not capture all people who experience menopause.
- More research is needed to explore how diverse genders experience menopause, and we hope that the information contained in our materials will help any person experiencing this life transition.

Menopause Terminology

- **Menopausal hormone therapy (MHT):** preferred term over hormone replacement therapy (HRT).
- **Genitourinary syndrome of menopause (GSM):** preferred term over vulvovaginal atrophy (VVA) because it is more comprehensive.
  - Includes dyspareunia, vaginal dryness/discomfort, dysuria, urinary frequency/urgency, recurrent UTIs.
- **Menopause Transition**: perimenopause + the first 12 months after the last menstrual period.
- **Menopause:** ≥ 12 months of amenorrhea.

RxFiles Menopause Newsletter pg 2: Menopause Overview

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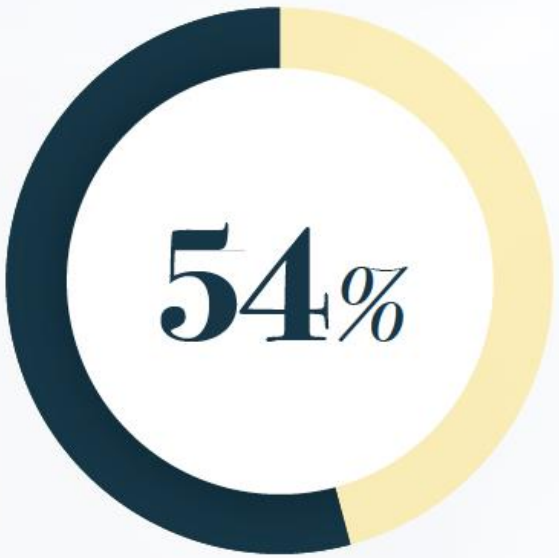
Still taboo after all these years.



Menopause remains shrouded in secrecy. More than half of women believe the topic is still taboo.

1 *in* 2

Women (46%) feel unprepared for perimenopause/menopause

55%

Wish they had learned about it earlier in life

This indicates the need for more education and awareness so the estimated 10 million women in Canada over the age of 40 who are menopausal (perimenopause/menopause/postmenopause) are well-informed.

4 in 10 women (38%) feel alone during menopause.

The Silence and the Stigma: Menopause in Canada. **October 2022**.

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Vasomotor Symptoms (VMS)

- VMS affects ~80% of women; severe/bothersome symptoms affect up to 20% of women. VMS can persist ~7-11 years.

PRACTICE POINT

Measuring serum estradiol, estrone, or SHBG is not recommended as they do not correlate with menopausal symptoms. NAMS 2022

- **<u>1st Line Therapy</u>**: Systemic MHT
  - ↓ frequency and severity of VMS by ~70-95%
- **<u>2nd Line Therapy</u>**: Non-Hormonal Therapy

✕ MHT Contraindicated

- Unexplained vaginal bleeding
- Acute liver disease
- Clotting disorder (e.g. factor V Leiden)
- Hx of CHD (CAD, stroke, TIA, unprovoked VTE, PAD) or at high-risk of CHD*
- Personal hx of estrogen-dependent CA (breast, endometrial, ovarian) or at high-risk of breast CA**
- Moderate risk of CHD*/breast CA** <u>and</u> age ≥60yrs <u>and</u> ≥10yrs since LMP

RxFiles Menopause Newsletter pg 2: Menopause Overview

Who is a candidate for systemic MHT?

Systemic hormone therapy is **very effective** for treating vasomotor symptoms (e.g. ⬇ hot flashes by 70-95%);[12] however, there are potential harms.[13] Canadian 2021 guidelines recommend hormone therapy as first line for women under the age of 60 or within 10 years of their last menstrual period (if no contraindications).[1] The back page of this newsletter helps weigh the benefits and risks of treatment.

✓ Consider MHT

- Age <60yrs or <10yrs since LMP and low risk (no cautions or contraindications)

RxFiles Menopause Newsletter pg 1 & 2: Cover page and Menopause Overview

? MHT Cautioned

- Moderate risk of CHD* and/or CV risk factors (smoking, HTN, DM, dyslipidemia, obesity) in ♀ age <60yrs or <10yrs since LMP
- Migraine with aura
- Hx of gallstones

Consider transdermal estrogen. *Expert opinion. Observational data suggest transdermal may ↓ risk of VTE (RR 0.61; 0.53-0.71), stroke (RR 0.81; 0.68-0.97) and gallstones (RR 0.79; 0.74-0.84) vs oral estrogen.* NAMS '22, *20-22*

- Moderate risk of breast CA** in ♀ age <60yrs or <10yrs since LMP

Consider non-hormonal tx. *MHT 2nd line after individualized risk assessment.* *Expert opinion. NAMS '22, 69, 70*

- Age ≥60yrs and ≥10yrs since LMP

Consider non-hormonal tx. *MHT 2nd line after individualized risk assessment.* *Expert opinion.* NAMS '22

Assessing Baseline Risk

- **Framingham Cardiovascular Risk Score (FRS) 10yr risk**:

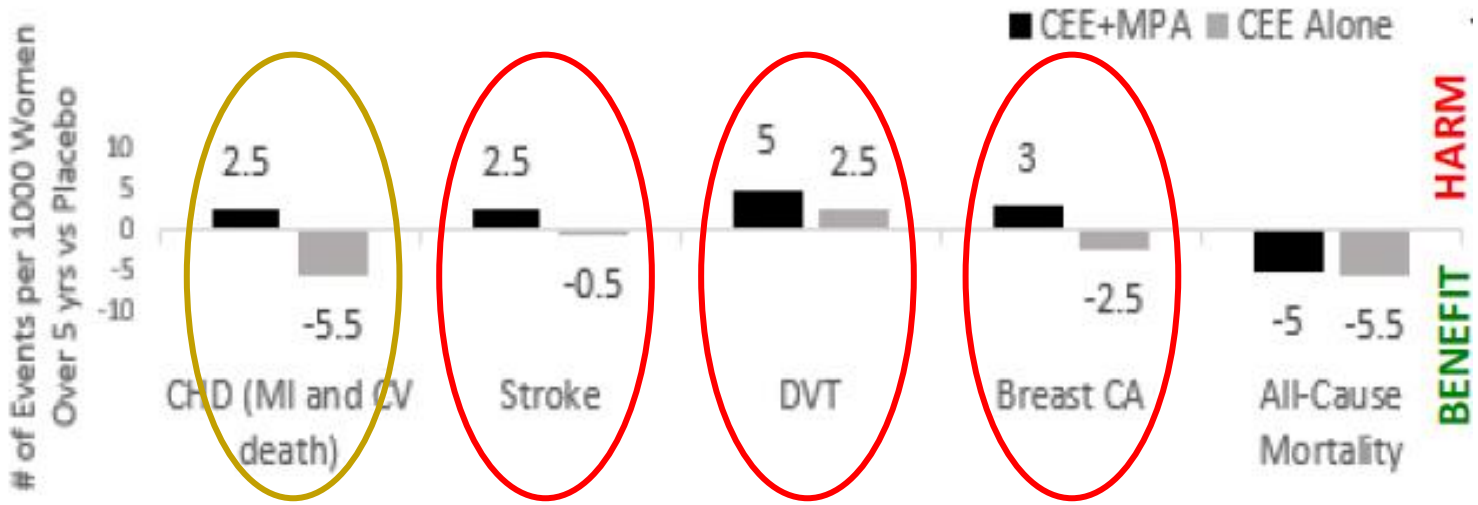
  low <10% | moderate 10-20% | high >20%

- **Breast Cancer Risk Assessment Tool (BCRAT) 5yr risk**:

  low <1.67% | moderate 1.67-5% | high >5%

- These risk calculators may support decision making but were not designed or validated for MHT.

WHI 2013: Subgroup Analysis
Risk Estimate of using MHT for 5 years; Age 50-59. (per 1000 women)



Inconsistent results across multiple studies

Consistent results across multiple studies

Figure 2. Benefits & Harms of MHT for ♀ aged 50-59 (subgroup analysis)[7]
Data is from the WHI intervention phase (2013 analysis). Note: these subgroup analyses are not statistically significant; however, they are the best available estimates at present.

RxFiles Menopause Newsletter pg 2 & 5: Menopause Overview & Efficacy and Safety of MHT

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VMS: Navigating Benefits and Harms

- **800 in 1000 women will have their hot flashes improve ≥50%.**

Women WITH a uterus (progestogen required)	
If < 60 years old:	If ≥ 60 years old:
Estrogen + Progestogen	**Estrogen + Progestogen**
Around **11 in 1000** (NNH=91) women will have a **major harm** (such as a stroke, a blood clot, or breast cancer) after 5 years.	Around **16 in 1000** (NNH=63) women will have a **major harm** (such as a stroke, a blood clot, or breast cancer) after 5 years.
Around **7 in 1000** (NNT=143) women will receive a **major benefit** (such as preventing a hip fracture or preventing colorectal cancer) after 5 years.	Around **7 in 1000** (NNT=143) women will receive a **major benefit** (such as preventing a hip fracture or preventing colorectal cancer) after 5 years.

Women WITHOUT a uterus	
If < 60 years old:	If ≥ 60 years old:
Estrogen	**Estrogen**
Around **3 in 1000** (NNH=333) women will have a **major harm** (such as a blood clot) after 5 years.	Around **13 in 1000** (NNH=80) women will have a **major harm** (such as a blood clot or stroke) after 5 years.
Around **15 in 1000** (NNT=64) women will receive a **major benefit** (such as preventing colorectal cancer) after 5 years.	Around **10 in 1000** (NNT=95) women will receive a **major benefit** (such as preventing a hip fracture or preventing colorectal cancer) after 5 years.

These risk estimates are the best that are available,[WHI 2013] but do have some uncertainty:

- For example: the estrogen studied was **conjugated equine estrogen** (**PREMARIN**) **0.625mg** for ~5-7 yrs; a lower dose, different formulation or shorter duration of therapy may result in lower risk.

Women at the **lowest risk are those under the age of 60 or within 10 years of their last menstrual period**. The benefits of MHT generally outweigh the harms for healthy, symptomatic women in this population.

RxFiles Menopause Newsletter pg 12: Vasomotor Symptoms Infographic

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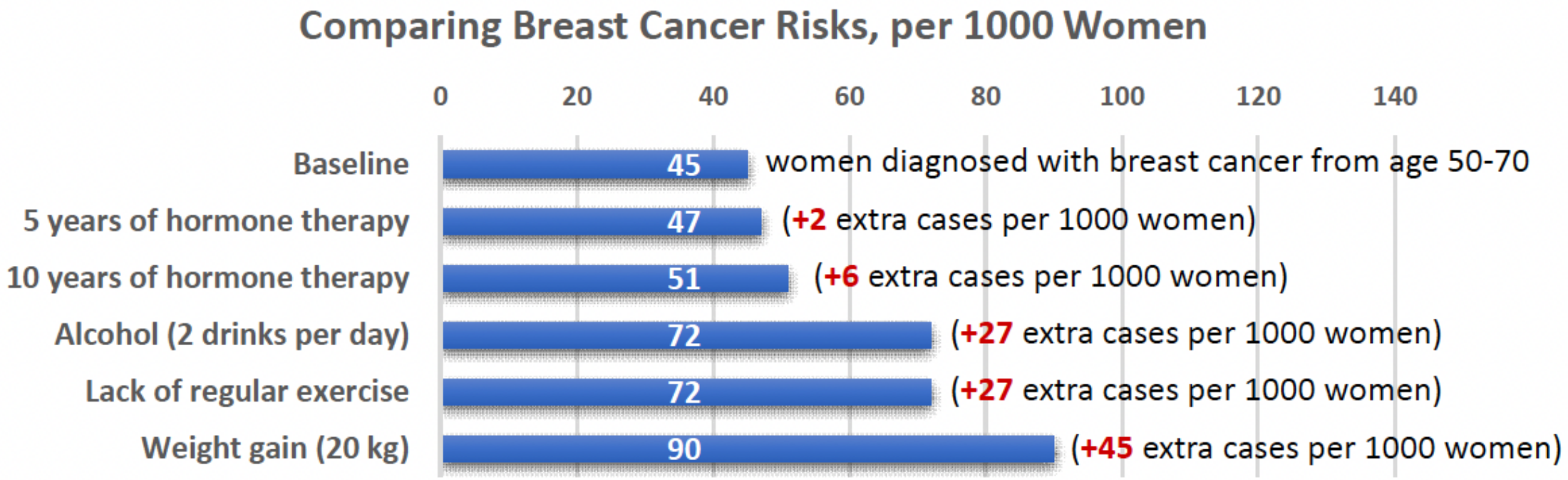
Breast Cancer Risk in Perspective



PRACTICE POINT

For women without a uterus and taking only estrogen, the WHI trial showed no increase in breast cancer. WHI 2013

SIGMA Canadian Menopause Society. **MENOPAUSE Times Have Changed. Let's Talk.** Pages 1-9.

Will systemic MHT help with other issues?

? Mood changes	Limited evidence (small RCT data) suggests estrogen therapy may be effective in the management of depressive disorders during **perimenopause.** **See Menopause FAQ pg 9 for details**.
? Sleep disturbances	↑ sleep quality and satisfaction in women with bothersome VMS. Limited evidence suggests that MHT may improve sleep independent of VMS.
✗ Sexual desire	Largely neutral effect on sexual desire. **See Menopause FAQ pg 9 for details.**
✗ Weight gain	Neutral effect on weight; may ↓ visceral fat and ↑ lean body mass.
✗ Cognitive concerns	Neutral in perimenopause and early post-menopause. May ↑ risk of dementia when initiated in older **post-menopausal women ≥65yrs**; **NNT=114**/4 years.[WHIMS] **See Menopause FAQ pg 8 for details.**

PRACTICE POINT

Counselling points:

- Mood and sleep *may* improve.
- Effect on sexual desire is *unpredictable*; some women will note benefit, others won't.
- Effect on weight is neutral.
- Effect on cognition appears neutral when started in women < 65 years.

RxFiles Menopause Newsletter pg 2 & 5: Menopause Overview & Efficacy and Safety of MHT

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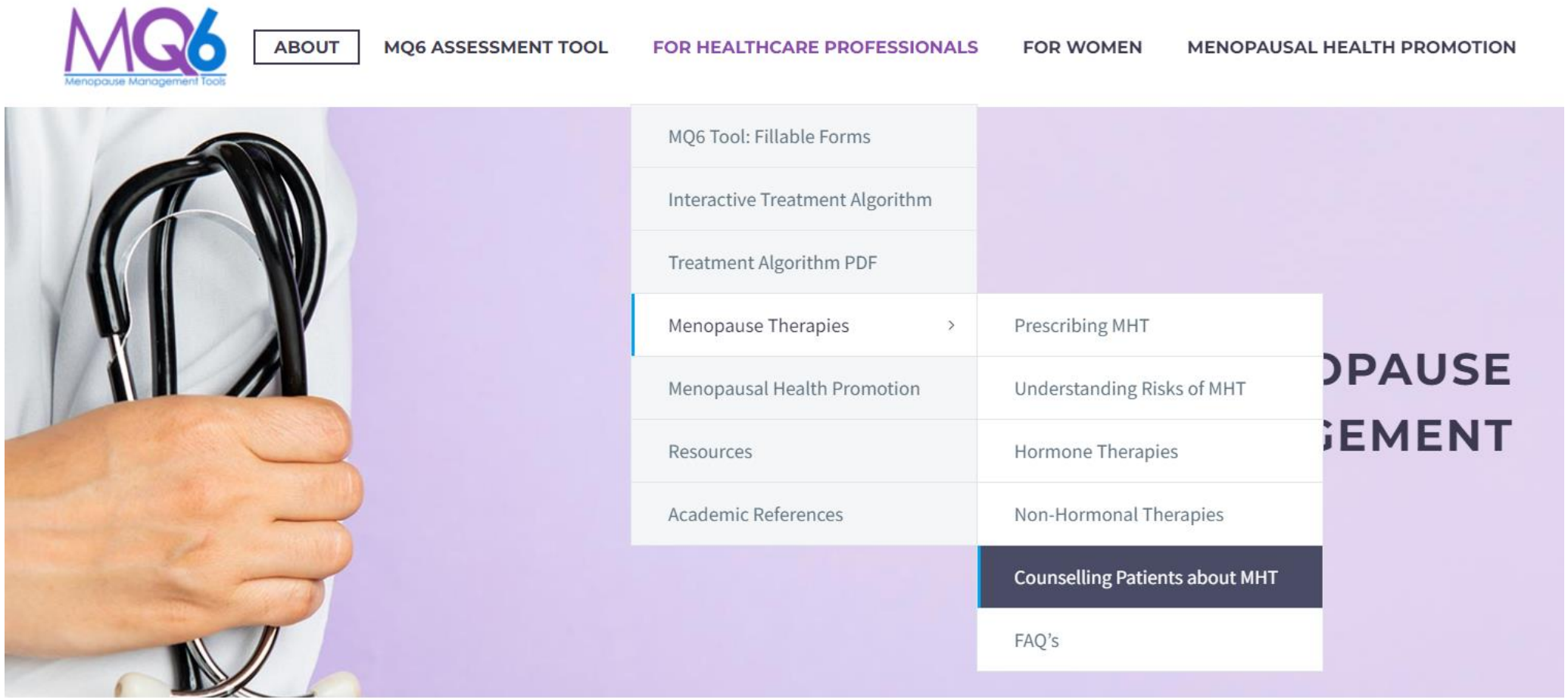
Counselling Patients on MHT



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Counselling Patients on MHT

- ☐ Menopausal Hormone Therapy (MHT) will likely be effective for your hot flashes and/or night sweats
  - ☐ Effects may take up to 4-8 weeks to work depending on dosage
  - ☐ We may need to adjust dosages
- ☐ MHT will provide bone protection to prevent osteoporosis while you are taking it
- ☐ You may also derive some benefit to symptoms of GSM such as vaginal dryness, urinary frequency or recurrent urinary tract infections
  - ☐ Depending on dose, we may need to add in additional treatments that act locally on the vaginal and urinary tissues
- ☐ You may also benefit with respect to joint pains, mood, sleep and quality of life
- ☐ The effect on libido is unpredictable
- ☐ There are some risks to consider:
  - ☐ There is a small "rare" increased risk of breast cancer (1/1000 women for EPT) after approximately 5 years of treatment
    - ☐ This risk may change based on product and regimen we choose
    - ☐ This risk is similar to that caused by 1-2 alcoholic drinks a day or being overweight/obese
    - ☐ Although more cases of breast cancer have been observed, the data indicates no increase in the # of deaths from breast cancer
  - ☐ There is an increased risk of blood clots in the first 1-2 years of treatment: the risk is about 1/1000 women
- ☐ When initiating MHT in women your age, MHT is safe for the heart and there is no appreciable increase in stroke risk or dementia
- ☐ Most MHT regimens are weight neutral, however weight gain is a normal effect of aging, so optimize your diet and exercise
- ☐ Common side effects include breast tenderness, bloating and mild headaches which usually settle within a few weeks
- ☐ With cyclic regimens you may see a small withdrawal bleed
- ☐ As VMS may last anywhere from 5-10 years or more, we will review and revisit indications for treatment annually

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Systemic Estrogen

Systemic Estrogen [PREMARIN 0.3mg ≈ ESTRACE 0.5mg ≈ patch 25mcg][85]

		Generic / TRADE	Initial & Max Dosing	Cost/30d
ORAL		**Conjugated equine estrogen PREMARIN** 0.3, 0.625, 1.25mg tab	**Initial:** 0.3-0.625mg po daily **Max:** 1.25mg po daily	$17-18 $18
ORAL		**Micronized Estradiol-17β ESTRACE, g** 0.5ᴳ, 1ᴳ, 2ᴳ mg tab	**Initial:** 0.5-1mg po daily **Max:** 2mg po daily	$10-13 $18
TRANSDERMAL	PATCH	**Estradiol-17β** [matrix patch – can cut to ↓cost] ☎ ▼ **ESTRADOT** 25, 37.5, 50ᴳ, 75ᴳ, 100ᴳ mcg/day patch **OESCLIM** 25, 50mcg/day patch	**Initial:** 25-50mcg 2x/wk (e.g. M&F) **Max:** 75-100mcg patch 2x/wk *ESTRADOT = smallest patch size*	$36-37 $39-40
TRANSDERMAL	PATCH	**Estradiol 17β CLIMARA** [matrix patch – can cut] 25, 50, 75mcg/day patch ☎ ▼	**Initial:** 25-50mcg patch weekly **Max:** 75mcg patch weekly	$33-34 $36
TRANSDERMAL	GEL	**Estradiol-17β DIVIGEL** ☎ ▼ 0.25, 0.5, 1mg gel sachets (0.1%)	**Initial:** 0.25mg [1 sachet] daily to right or left upper thigh (alternating) **Max:** 1mg [1 sachet] daily	$40 $40
TRANSDERMAL	GEL	**Estradiol-17β ESTROGEL** 0.06% gel pump ☎ ▼	**Initial:** 1 pump [1.25g] to one or both arms daily (wait 2min pre clothes)	$56

DO NOT apply to breast. **AVOID** skin-to-skin transfer.

PRACTICE POINT

Guidelines and experts recommend transdermal products as the preferred treatment in those with CV risk factors, based on observational data.

Which systemic estrogen should I choose?

- Observational data suggests **transdermal** (gel & patch) may have ↓VTE risk, ↓gallbladder disease, ?improved sleep, & ?↑sex drive vs oral estrogen.[20-22]
  SK coverage ☎: intolerant to oral estrogen or fasting TG ≥4.5mmol/L.
- **Oral estradiol** may have ↓VTE risk vs conjugated equine estrogen.[93]

RxFiles Menopause Newsletter pg 3 & 5: Menopause Hormone Therapy & Efficacy and Safety of MHT

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Transdermal Patches (Systemic MHT)

Did you know?

- **The buttocks** is a preferred application site for an estradiol transdermal patch due to ↑ privacy & ↓ skin irritation.[5]

PRACTICE POINT

All estrogen-only patches can be cut, due to their matrix delivery system. This can be useful if patch strengths are shorted, or if cost is a barrier. The dosing interval remains the same.
Note: Do not cut the estrogen + progestogen (i.e. ESTALIS) patch.

Progestogen

A progestogen is required for all ♀ with a uterus & on systemic estrogen to ↓ endometrial cancer.

	Generic / TRADE	Usual Dosing	Cost/30d
ORAL	**Medroxyprogesterone** **PROVERA, g** 2.5§, 5§, 10§ mg tab	**If under the max estrogen dose**: 2.5mg po daily or cyclic: 5mg daily first 12-14 days each month **If on max estrogen dose**: 5mg po daily or cyclic: 10mg daily first 12-14 days each month	$9
ORAL	**Micronized progesterone** **PROMETRIUM, g** 100mg ☎ ▼ cap peanut oil in g Teva. sunflower oil in brand & g PMS.	**If under the max estrogen dose**: 100mg po HS or cyclic: 200mg HS first 12-14 days each month **If on max estrogen dose**: 200mg po HS or cyclic: 100mg po AM + 200mg po HS first 12-14 days each month	$18-30
IUD	**Levonorgestrel MIRENA** 52mg intrauterine device	**Off-label**: insert q5yrs.[50,51,87] Extended intervals unstudied. (Approved in Europe for women on any estrogen dose.)	$7 ($400 up front)

PRACTICE POINT

PROMETRIUM can be sedating, some find this beneficial to help with sleep. Counsel patients to take it at bedtime.

Which progestogen should I choose?

- Micronized progesterone **PROMETRIUM** ↑drowsiness and may ?↓VTE, ?↓CV , ?↓breast cancer risk vs medroxyprogesterone.[NAMS'22, 93, 102-104]
- **MIRENA** useful if oral progestogen not tolerated/inconvenient, contraception desired, or to help reduce heavy bleeding in perimenopause.

Continuous or cyclical progestogen?

- **Continuous dosing** avoids withdrawal bleed & often results in amenorrhea after 12 months → often preferred if last menstrual period >1yr prior. Switch to cyclic dosing if breakthrough bleeding persists throughout first 6 months.
- **Cyclic dosing** causes a monthly withdrawal bleed → useful during the menopause transition as helps reduce breakthrough bleeding. If heavy/erratic bleeding, ↑dose or switch to continuous.

RxFiles Menopause Newsletter pg 3 & 5: Menopause Hormone Therapy & Efficacy and Safety of MHT

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Did you know?

- The **levonorgestrel IUD MIRENA** has data for 5 years of endometrial protection (off-label).[6,7] Candidates include those who require contraception, do not tolerate an oral progestogen, prefer the convenience, or have perimenopausal heavy menstrual bleeding. It can be used for patients on any estrogen dose.

PRACTICE POINT

Although data supports the extended use of **MIRENA** up to 8 years for contraception, data only supports the use of **MIRENA** up to 5 years for endometrial protection in women on estrogen therapy.

RxFiles Menopause Newsletter pg 1 & 8: Cover page and Menopause FAQs

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Estrogen + Progestogen

- Combination products increase convenience, but can limit dose flexibility.

	Generic / TRADE	Strength	Usual Dose	Cost/30d
ORAL	Estradiol-17β + micronized progesterone BIJUVA	1/100mg cap	1/100mg po HS	$40
	Estradiol-17β + drospirenone ANGELIQ	1/1mg tab ✗ ⊗	1 tab po daily	$31
	Estradiol-17β + norethindrone ACTIVELLE	1/0.5mg tab, 0.5/0.1mg LD tab ✗ ⊗	1/0.5mg po daily	$97
	Bazedoxifene + conjugated estrogen DUAVIVE	20/0.45mg tab ✗ ⊗	1 tab po daily	$115
PATCH	Estradiol-17β + norethindrone ESTALIS	50/140mcg, 50/250mcg patch ☎ ▼	1 patch twice/week	$43

	Comments
ORAL	• Less flexibility with titrating/tapering doses vs individual products. • DUAVIVE (🇺🇸 USA: DUAVEE): Bazedoxifene is a tissue selective estrogen complex (TSEC). No progestogen needed; risk of endometrial cancer mitigated by TSEC. Useful if breast tenderness or if progestogen not tolerated.
PATCH	• Matrix patch, but avoid cutting as unstudied if adequate progestogen protection.

RxFiles Menopause Newsletter pg 3: Menopause Hormone Therapy (MHT)

Women Who Require Contraception + Treatment for VMS

- Consider a progestin-only contraceptive (+ systemic estrogen if needed for VMS) or low-dose CHC (e.g. LOLO, ALESSE).

PRACTICE POINT

Avoid CHCs for treatment of VMS in post-menopausal women, as the estrogen dose is ~3-6x higher than MHT.

Box 1: When to Stop Contraception. [1, MQ6.ca, expert opinion]

- Lab tests (e.g. FSH) are typically not recommended, as they fluctuate in perimenopause and can be misleading. No lab test shows definitive loss of fertility.
- In ♀ ≥ 50yrs, stop hormonal contraceptive; use non-hormonal contraception and monitor return of menses/emergence of VMS. Continue non-hormonal contraception until amenorrhea for > 12mo.
- In ♀ ≥ 55yrs, stop hormonal contraceptive. Spontaneous conception very rare.

Ask about vaginal health in women aged 45+ years.

- Normalize talking about vaginal health.
- Under-recognized and under-treated.
- Symptoms often ↑ over time & persist if untreated.

Women who have genitourinary menopause symptoms:[1] **~50%**

Women who ask a healthcare provider for help with these symptoms:[3] **~25%**

GSM affects women regardless of whether they are sexually active or not.

University of Saskatchewan

GSM Treatment Options

1st Line Therapy: vaginal moisturizers (e.g. **REPLENS, GYNATROF, REPAGYN**)

- Use routinely (e.g. ~3x/week); some prefer the viscosity of one over the other (e.g. **GYNATROF** thicker than **REPLENS**)

PRACTICE POINT

When suggesting an OTC product, remember "moisturizers are for maintenance, and lubricants are for love-making."

2nd Line Therapy: vaginal estrogen (cream, ring, tablet)

- ↓ GSM by ~60-80%; effects seen within 2-4 weeks, full effect after 3 months.
- **Vaginal estrogen is 1st line if** moderate to severe GSM or recurrent UTIs.

RxFiles Menopause Newsletter pg 3: Menopause Hormone Therapy Drug Comparison Chart

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Vaginal Estrogen (low-dose)

- Before initiating, GSM should be confirmed via physical exam to rule out other causes and/or vaginal/endometrial risk factors.[expert opinion]

CREAM	**Conjugated equine estrogen PREMARIN** 0.625mg/g vaginal cream (rose-scented)	0.5-2g vaginally HS x 2 weeks, then ↓ to 1-3x per week	$10 ($34/30g)
	Estrone ESTRAGYN 1mg/g vaginal cream (unscented)	0.5-2g vaginally HS x 2 weeks, then ↓ to 1-3x per week	$10 ($48/45g)
RING	**Estradiol-17β ESTRING** 2mg vaginal ring (releases 7.5mcg/day) Note: USA **FEMRING** releases 50-100mcg/day for VMS	Insert 1 ring vaginally q 90days	$32 ($96 up front)
TAB	**Estradiol-17β VAGIFEM** 10mcg vag tab	1 tab vaginally HS x 2 weeks, then ↓ to 1-3x per week	$30-70
	Estradiol-17β IMVEXXY 4, 10mcg softgel		$27-58

PRACTICE POINT

Vaginal estrogen can be used together with systemic estrogen in women who have both VMS and GSM.

Which vaginal estrogen should I choose?

- **Efficacy**: all are similar.[84] Creams have an initial advantage if severe vaginal atrophy/dryness, to help heal (may feel initial tingling). Creams can also be applied externally off-label (e.g. to clitoris, labia).
- **Systemic exposure**: minimal for all options, but likely cream > tab ≈ ring.[52]
- **Cost**: creams typically lowest cost (e.g. 1gram 2x/week ≈ $10/month on average).
- **Convenience**: vaginal ring q3 months an advantage. Tab can be less messy than a cream.
- Rose-scented **PREMARIN** can be irritating to vaginal mucosa for some patients.

RxFiles Menopause Newsletter pg 3 & 6: MHT Drug Comparison Chart & Efficacy and Safety of MHT

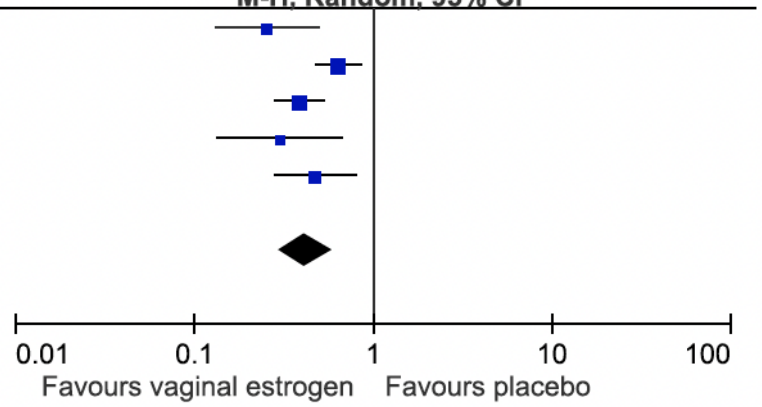
Vaginal Estrogen for Recurrent UTIs

Vaginal estrogen may reduce the risk of recurrent UTIs vs placebo in post-menopausal women:

- Meta-analysis of RCTs (N=5, n=1936) showed a reduction of recurrent UTIs:
  - ❖ RR=0.42 (95%CI = 0.30-0.59), **NNT=7** over 6-12 months.
- Oral estrogen was not effective at reducing recurrent UTIs vs placebo.

Study or Subgroup	vaginal estrogen Events	Total	placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Raz 1993	8	50	27	43	15.0%	0.25 [0.13, 0.50]	1993
Eriksen 1999	27	53	44	55	27.4%	0.64 [0.47, 0.86]	1999
Simunic 2003	49	828	120	784	26.6%	0.39 [0.28, 0.53]	2003
Dessole 2004	6	44	20	44	12.0%	0.30 [0.13, 0.68]	2004
Ferrante 2019	8	18	16	17	19.1%	0.47 [0.28, 0.80]	2019
Total (95% CI)		**993**		**943**	**100.0%**	**0.42 [0.30, 0.59]**	
Total events	98		227				

Heterogeneity: Tau² = 0.09; Chi² = 11.09, df = 4 (P = 0.03); I² = 64%
Test for overall effect: Z = 4.88 (P < 0.00001)



Chen YY et al. *Int Urogynecol J*. 2021;32(1):17-25.

RxFiles Menopause Newsletter pg 6: Efficacy and Safety of MHT; Benefits and Harms of Vaginal Estrogen

University of Saskatchewan

Did you know?

Despite overwhelming safety data, vaginal estrogen products still carry the same black box warnings as systemic MHT.

• Vaginal estrogen is minimally absorbed at commercially available low doses. **Vaginal estrogen does not appear to increase the risks of harms such as breast cancer, endometrial cancer, or cardiovascular disease.**[11] Therapy can be continued for as long as benefit is perceived by the patient.[10] See page 7 for more info.

PRACTICE POINT

When counselling patients, advise that the black box warnings on the product label do not apply to low-dose, vaginal estrogen products. Low-dose vaginal estrogen does not require a progestogen.

RxFiles Menopause Newsletter pg 1 & 7: Cover page and Menopause FAQs

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Are there any contraindications to vaginal estrogen?

- Use is contraindicated in women with undiagnosed vaginal/uterine bleeding and should be used with caution in women with estrogen-dependent neoplasia.[NAMS 2020]

PRACTICE POINT

Low-dose vaginal estrogen can be used even if contraindication to systemic estrogen.

3. Can vaginal estrogens be used to treat GSM in those with a history of breast cancer?

Observational data shows no increased risk of breast cancer recurrence with use of low-dose vaginal estrogens in individuals with a history of breast cancer. However, non-hormonal options (i.e. vaginal moisturizers and lubricants) should be offered first-line, before considering vaginal estrogen therapy in consultation with the oncologist.[NAMS 2020, ACOG 2016, BMS 2020, KSM 2020, 44]

- Observational trials investigating the use of vaginal estrogens in patients with a history of breast cancer have shown no increased risk of breast cancer recurrence. These results appear consistent for patients who are receiving tamoxifen.[40-42]
- Clinical trials are currently ongoing to assess the safety of vaginal estrogen products in those taking aromatase inhibitors.[66]
- There is a lack of long-term safety data for vaginal estrogen use in patients with a history of breast cancer; a shared decision-making approach should be used involving both the patient and their health care team.[47]

RxFiles Menopause Newsletter pg 7: Menopause FAQs

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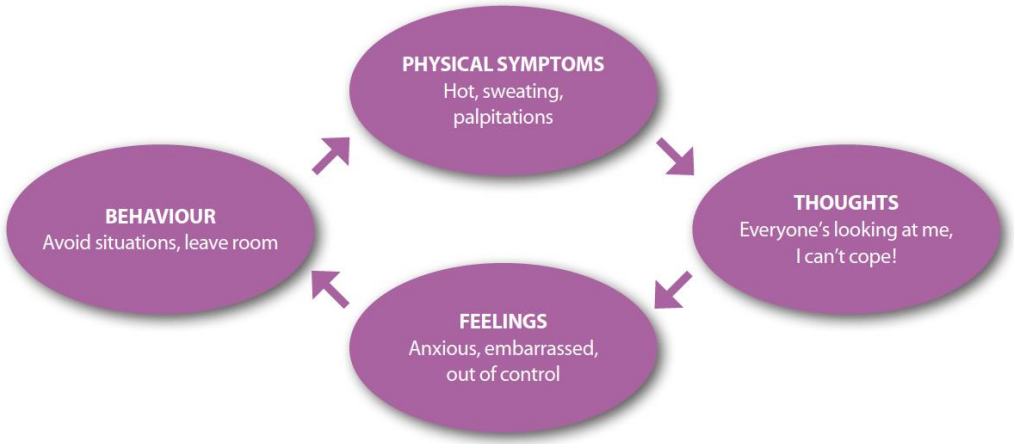
CBT for Menopause Therapy

CBT for Menopause Therapy (British Menopause Society 2023)

https://www.womens-health-concern.org/wp-content/uploads/2023/02/02-WHC-FACTSHEET-CBT-WOMEN-FEB-2023-A.pdf

CBT for hot flushes focuses on the links between:



Cognitive and behavioural strategies ***Paced breathing*** is an important part of the CBT approach for hot flushes. As with any skill it requires regular practice – breathing from your stomach. At the onset of a flush – ***relax your shoulders*** – ***breathe slowly from your stomach*** – ***concentrate on your breathing***. Paced ***breathing*** involves focusing on your breathing, accepting that the hot flush will pass and just ***letting the hot flush flow over you***.

Cognitive (thinking) strategies – women's main types of worries about hot flushes and night sweats tend to be:

1. Social embarrassment (especially around men, younger people and at work) – *"Everyone's looking at me" – "I look terrible".*

Night sweats and sleep problems can be particularly challenging to deal with given the negative impact that night sweats can have on sleep. Research studies with women going through the menopause have found that worrying at night about sleeplessness and its effects on the following day (tiredness, wellbeing and performance) can lead to anxiety which then makes sleep less likely. Therefore, managing sleep and night sweats requires a two pronged approach:

1. creating good habits to optimise ***sleep behaviour and environment***, and
2. applying the cognitive behavioural work for hot flushes to develop ***calmer thinking and behavioural responses*** when sleep is disrupted due to night sweats.

Prescription Options for VMS

- Considered for those who are not candidates for MHT (i.e. contraindicated) or those with a preference for non-hormonal options.
  - ❖ All are less effective than systemic MHT.
  - ❖ Consider comorbidities such as depression, insomnia, neuropathy and urinary incontinence.

There are no head-to-head trials of these agents, and efficacy is confounded by the **large placebo effect (which can ↓ hot flashes 20-50%).**

	Generic Name; BRAND Name	Dosing for VMS	$/30d
SSRI	Paroxetine PAXIL, g USA: 7.5mg cap HS BRISDELLE	10-20mg po daily	$20
SSRI	Citalopram CELEXA, g	10-20mg po daily	$14
SSRI	Escitalopram CIPRALEX, g	10-20mg po daily; See comments.	$20
SNRI	Venlafaxine EFFEXOR XR, g	37.5-75mg po daily	$15
SNRI	Desvenlafaxine PRISTIQ ER, g ✗ ⊗	100-150mg po daily	$92
Gabapentinoid	Gabapentin NEURONTIN, g	Initiate 100-300mg HS, ↑ 100mg q3-4 days up to 900mg HS.[SOGC'21]	$13-15
Gabapentinoid	Pregabalin LYRICA, g	150-300mg po HS	$24
Other	Clonidine CATAPRES, g	0.025-0.05mg po BID	$15
Other	Oxybutynin DITROPAN, g	2.5-5mg po BID	$14

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Did you know?

• Although less effective than hormones, **select SSRIs and SNRIs** have shown benefit for treating vasomotor symptoms (see page 4). **The dose needed is typically lower** than for anxiety or depression (& higher doses are often no more effective).

PRACTICE POINT

VMS benefit is not a SSRI/SNRI class effect.
Onset of effect is often within days.
If one SSRI/SNRI is ineffective, it is reasonable to try another SSRI/SNRI before moving to another class of medication.

	Generic Name; BRAND Name	Dosing for VMS	$/30d	Adverse Events AE Drug Interactions DI	Efficacy for VMS vs placebo	Evidence & Comments Start low and titrate to ↓ AE. Review need for therapy annually.
SSRI	Paroxetine PAXIL, g USA: 7.5mg cap HS BRISDELLE	10-20mg po daily	$20	See Rxfiles: Antidepressants, pg 178 • AE: nausea, HA, drowsiness, dizziness, dry mouth, ↓ libido, (SNRI ↑ AE vs SSRI). • DI: paroxetine & fluoxetine: ↓ tamoxifen levels due to CYP2D6 inhibition (contraindicated).	SSRI/SNRI ↓ by 27-65% composite of hot flash severity & frequency.[4,28] Often onset in days (vs weeks for depression).[31]	• Low doses often sufficient, higher than studied doses unlikely to offer further VMS reduction benefits. • If one SSRI/SNRI is ineffective or not tolerated, another SSRI/SNRI with evidence of efficacy can be tried before moving onto another class of medication. May also improve mood and/or sleep. • Fluoxetine & sertraline: Not usually recommended as no difference vs placebo for hot flash efficacy.[28] • Paroxetine: Most well studied; ↓ VMS by ~40-65%.[4,29] Discontinue slowly to avoid withdrawal sx. • Escitalopram: Reasonable to initiate at 5mg/day, but this dose is not studied for VMS efficacy.[NAMS'23] • Venlafaxine: ↓ VMS by ~40-65%.[4] 37.5mg daily improved VMS in ~1 wk; 75mg daily improved sleep.[29,30] 1st line non-hormonal in breast CA pts,[SOGC'21] due to superiority vs gabapentin.[91] D/C slowly to ↓withdrawal. • Duloxetine 60mg:↓ VMS similar to escitalopram 20mg; but small, short term RCT (12 weeks).[82]
SSRI	Citalopram CELEXA, g	10-20mg po daily	$14			
SSRI	Escitalopram CIPRALEX, g	10-20mg po daily; See comments.	$20			
SNRI	Venlafaxine EFFEXOR XR, g	37.5-75mg po daily	$15			
SNRI	Desvenlafaxine PRISTIQ ER, g ✗ ⊗	100-150mg po daily	$92			

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BE WHAT THE WORLD NEEDS

Gabapentinoids

Gabapentinoid	**Gabapentin** NEURONTIN, g	Initiate 100-300mg HS, ↑ 100mg q3-4 days up to 900mg HS.[SOGC'21]	$13-15	See RxFiles: Seizures, pg 164 • **AE**: dizziness, drowsiness. • **DI**: ↑ risk of respiratory depression with opioids.[42]	**Gabapentin ↓ by 45-71%** hot flash frequency;[34,35] onset within 1 week.[35]
	Pregabalin LYRICA, g	150-300mg po HS	$24		

- Gabapentin: Useful if hot flashes causing insomnia or night awakenings, as HS dosing can cause drowsiness and facilitate return to sleep. AE most pronounced during first 1-2 weeks, improves within 4 weeks.[34,36] Dosing up to 900mg/d used in clinical trials,[83] but titrate to lowest effective dose.
- Pregabalin: Not generally recommended due to limited evidence (one 6 week RCT).[37,NAMS 2023]

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Other Options

Other	**Oxybutynin** DITROPAN, g	2.5-5mg po BID	$14	• AE: dry mouth 52%,[39] GI upset, constipation, blurred vision.	↓ **by 60-77%** hot flash frequency, onset ~1 wk.[40]
	Clonidine CATAPRES, g	0.025-0.05mg po BID	$15	• AE: dizziness, dry mouth, hypotension, sedation, HA.	↓ **by 20-40%;**[4] limited evidence; mixed results.

- Oxybutynin: Small RCTs show efficacy over 6 and 12 weeks.[39,40] AE common (e.g. anticholinergic); observational data suggests concerns about cognitive decline in older women.[41]
- Clonidine: Not generally recommended due to AE & less effective than SSRI, SNRI, and gabapentin for relief of VMS.[28,38, SOGC'21, NAMS'23] Discontinue slowly to avoid withdrawal symptoms.

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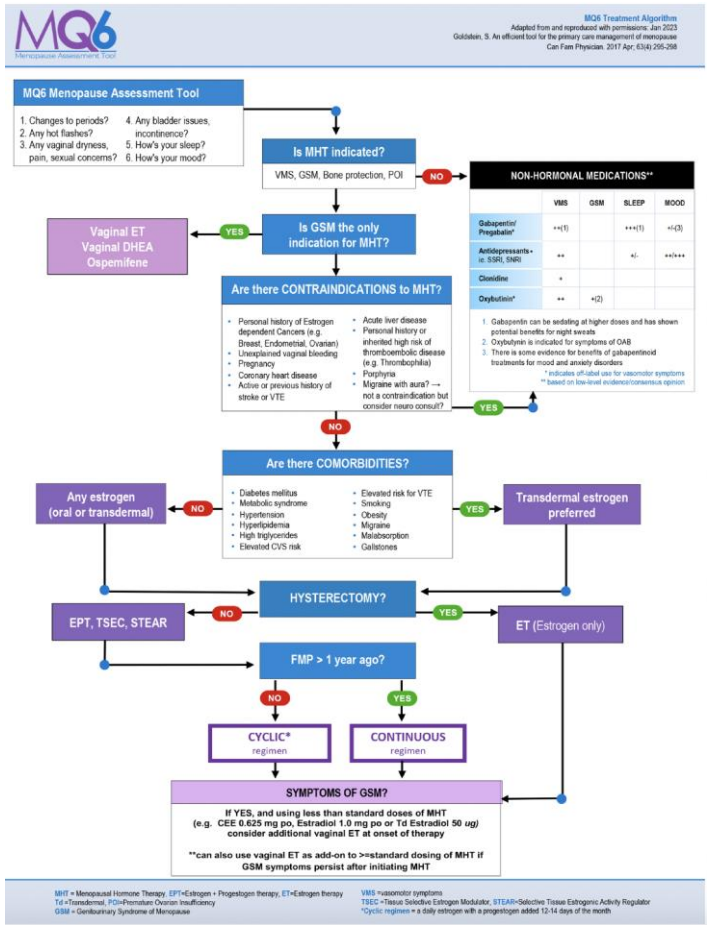
Menopause Quick 6 (MQ6) Assessment Tool

ASSESSING THE MENOPAUSAL PATIENT: THE MENOPAUSE QUICK 6 SCREEN (MQ6)

Key questions to ask perimenopausal and menopausal women in assessing their need for treatment.

1. Any changes in your periods?
2. Are you having any hot flashes?
3. Any vaginal dryness or pain or sexual concerns?
4. Any bladder issues or incontinence?
5. How is your sleep?
6. How is your mood?

Treatment Algorithm:



RxFiles Menopause Newsletter pg 10: MQ6 algorithm

www.mq6.ca

BE WHAT THE WORLD NEEDS

University of Saskatchewan

Other Menopause Resources

- **For Providers:**
  - **SIGMA Pocket Guide**
  - **MHT Counselling List**
  - **Menopause Rating Scale**
- **For Patients:**
  - **NAMS MenoNotes**
  - **Gynaecology QI Collaboration**
  - **SOGC Menopause & U**

Thank you!

Please fill out your session evaluation now!

#myfmf

FamilyMedicineForum

FamilyMedForum

FamilyMedForum

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