Menopause Panel Cases & Key Messages

Amy G. Cantor MD, MPH & Moira Ray MD, MPH Women's Health Primary Care Update
May 16th, 2025



Case 1: Perimenopausal Symptoms

- 47-year-old who reports lengthened menstrual cycle, 3 days of bleeding. Mainly concerned about sleep disruption, frequent hot flashes, night sweats waking her up multiple times every night.
- She is wondering what is causing these symptoms?



Stages, Symptoms and Health Effects

The Three Stages of Menopause



Perimenopause

2-8 years before menopause; symptoms can include hormonal changes, irregular menstruation, and hot flashes



Menopause

The point in time twelve months after a woman's last period



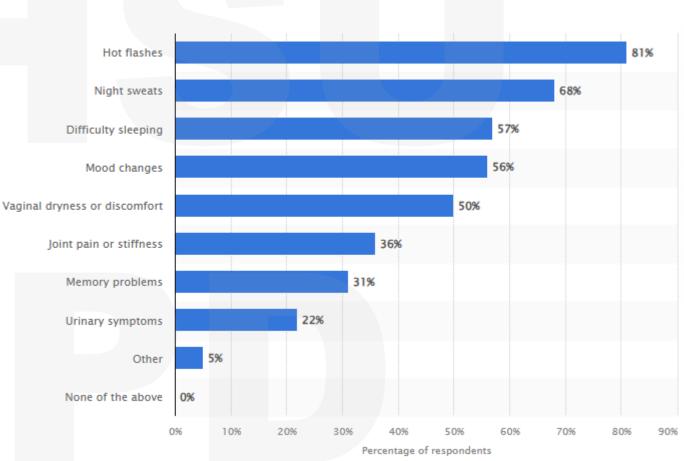
Postmenopause

Symptoms may ease; health changes include increased risk for osteoporosis and heart disease

Symptoms Associated with Menopause

Percentage of menopausal or postmenopausal women in the United States who experienced select menopause symptoms as of 2023

- Survey of 2,000 U.S women



Tip 1: Symptom Inventory

- No laboratory test is predictive or diagnostic of perimenopause
- Symptom scoring tools can help guide conversations and track treatment effects
- The Menopause Rating Scale is available in Epic/EMR

Which of the following symptoms apply to you at the each symptom. For symptoms that do not apply, possible symptoms:				appropriate	box for	
Symptoms:						
		none	mild	moderate		very severe
	Score	= 0	1	2	3	4
•						
 Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early) 						
in performance, impaired memory, decrease in concentration, forgetfulness)						
sexual activity and satisfaction)						
in the vagina, difficulty with sexual intercourse)						
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֡	(episodes of sweating)	Hot flushes, sweating (episodes of sweating)	Hot flushes, sweating (episodes of sweating)	Hot flushes, sweating (episodes of sweating)	Hot flushes, sweating (episodes of sweating)	Hot flushes, sweating (episodes of sweating)

Menopausal Rating Scale (MRS)

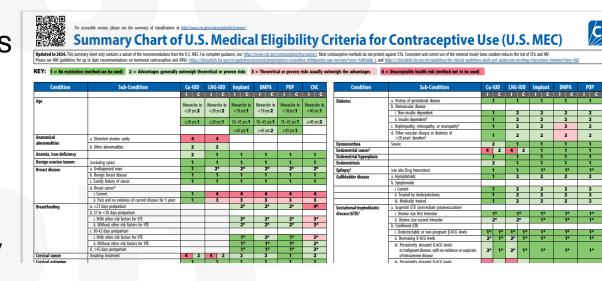
Case 2: Options for Perimenopausal Symptom Management

- Pregnancy considerations
- Other risk factors or comorbidities
- Hormonal vs nonhormonal treatment options



One Key Question: "Would you like to become pregnant in the next year?"

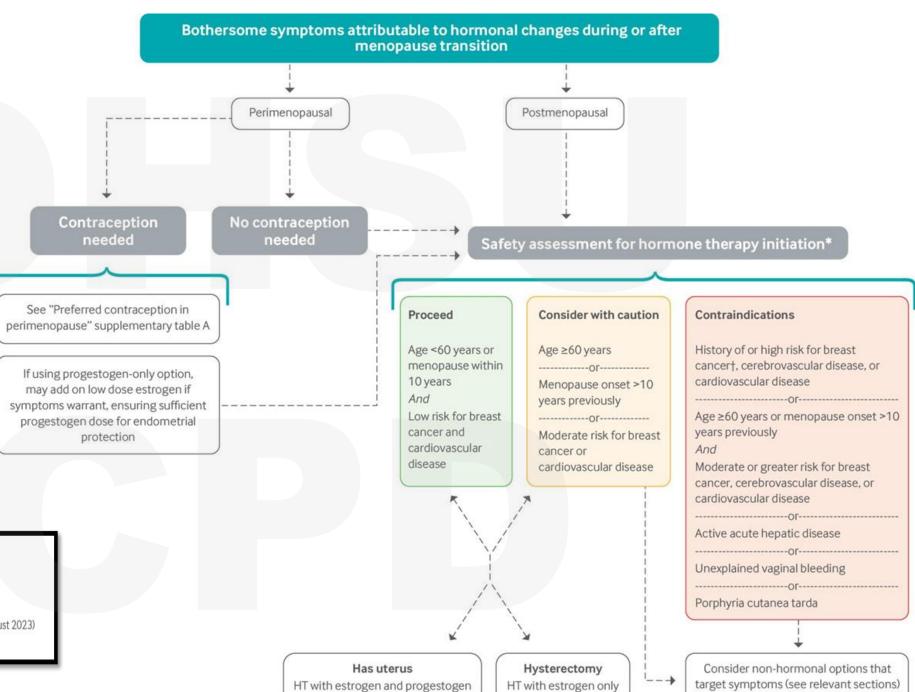
- If patient is menstruating and at risk of pregnancy, discuss contraception methods (e.g., combined oral contraception [coc], progestin only pills, IUDs, implants, etc).
- Consider individual risk factors to determine best contraceptive choice.
- COCs are at greater doses than commonly used for menopausal hormone therapy.



https://www.cdc.gov/contraception/media/pdfs/2024/07/us-mec-summary-chart-color-508.pdf



Approach to Starting HT



Clinical Review » State of the Art Review

Management of perimenopausal and menopausal symptoms

BMJ 2023; 382 doi: https://doi.org/10.1136/bmj-2022-072612 (Published 08 August 2023) Cite this as: BMJ 2023;382:e072612

Hormone Therapy: Indications for Use

- Vasomotor symptoms (VSM): Bothersome hot flashes and night sweats.
- Genitourinary symptoms (GSM): Vulvovaginal and bladder symptoms.
- Osteopenia: Prevention of bone loss and reduction of fracture risk.
- Surgical or premature menopause: Menopause in someone aged younger than 40 years: "HRT"
- But <u>NOT</u> for: prevention of cardiovascular disease or dementia; management of MSK conditions; management of hair loss, weight gain, etc.

Tip 2: Patient Resources

CREATE MY MENOPLAN

This personalized tool can help you narrow your search for treatments and coping strategies.

- Click on the symptoms that bother you, to see the treatments that are known to help or may help.
- If you want to read more about symptoms, go here.

Pick Up To 6 Symptoms





























Get Treatments for Selected Symptoms!

https://mymenoplan.org/create-my-menoplan/

Case 3: Risks and Benefits of HT

- 49 yo with LMP at age 47
- Has been on CEE and MPA for bothersome hot flashes for 4 years.
- Recently spoke with her mom who told her HT was going to give her heart attack.
- She wants to know if HT is safe for her?



Key Findings from Women's Health Initiative

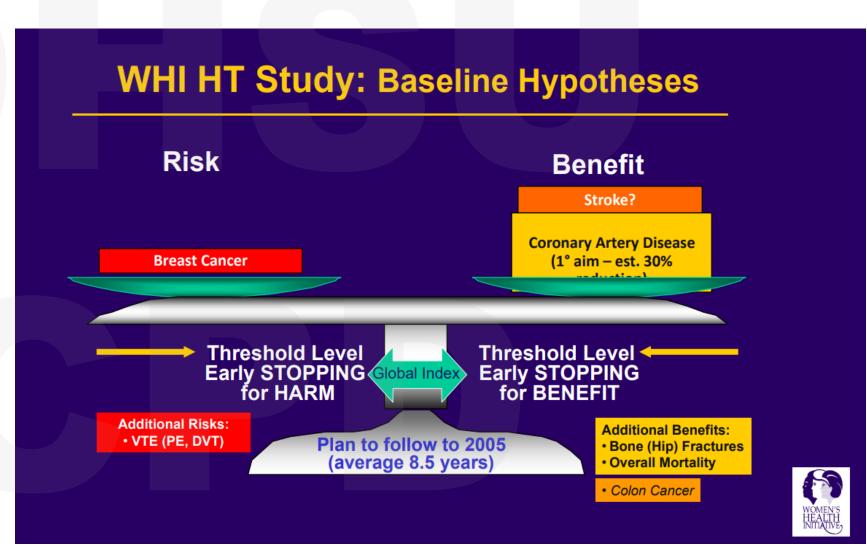
RCT, n=27,000 women:

- Hysterectomy: CEE vs.
 Placebo
- Uterus in place: CEE + MPA vs. Placebo

Primary outcome:

Cardiovascular disease

Avg. Age = 63 years



FINANCIAL REVIEW

Menopause drug scare

600,000 women warned to stop combined 11x 1 medicaubi

Hormone alert for cance

True degree of therapy risk lost in the clamour of commentate

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HRT linked to cancer and stroke:

Expert panel backs HRT cancer warning

AUSTRALIAN women have been warned to fruit. their one of hormon restamment therapy to perment, beaut disease and atroke to no more than theree years, after an expert committee last religible baseland TS exposures over the long term safety of BORT.

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HORMONE THERAPY

THE RISKS

41% increase in strokes; 29% in crease in teart attacks; doubling of renous blood dots; 26% ingrasse in breast cancer.

doctors demand drug restrictions

THE BENEFITS

37% suit in colorectal cancer; onethird reduction in hip fractures: 24% reduction in all fractures. Invested of the Emprison Madical

National Institutes of Health, was don to be completed in 2005 but was stopped. after the women were followed for an

outweighed the benefits, only a small number of individual women - about

> 2.5 per cent - had problems. Compared with women taking a placebo, forevery 10,000 women taking combined HRT eight more

womin aged 50 to 79.

of get breast cancer, seven more swheart artacks, eight more

Whenen's Health Initiative run by the US

average of \$.2 years. It involved \$6.600.

In the Journal of the American Medical

Amodorium, Although the risks overall

The results were published yesterday

More needed to settle HRT scare

The hormone replacement therapy scare inspired lot month by US sesearchers is having predictable results. Australia's higgest supplier of the oestrogen-progestin combination has reported a 30 per cent decline in sales since Americas doctors cut short a long-term study of 16,000 HRT users to warn the world that the therapy increased the tisks of breast cancer, heart disease, stroke and blood clots, particularly among women who took the therapy for five years or more. A Melbourne specialist went further, claiming two-thirds of his patients had quit HRT. These outcomes will suit, if not fully satisfy, doctors who embraced the US warnings. What has not been answered is whother docors too quiddy raind out HET for weenen trying to prevent or minumise the debilitating symptoms of menopusse, including sweats, sleeplesssess, hot flushes and deterioration in bone density.

For the defenders of HRC, the American report prompted understandable panic among its users. This might have been avaided, or at least lessened, had the researchers not highlighted their findings with a simplistic, misleading and, arguably, mischievous set of statistics. The ersuing furore left little room, for instance, to course argaments such as women being twice as likely to develop breast cancer if they sook two alcoholic drinks a day, instead of HRC. The American report sold on HRC wee's broast cancer risk, for example, jumped 26 per cent (with similarly alumning rises in the risks of other side effects). To women who know little about statistical interpretation, this might (and probably did) suggest their odds of developing breast cancer would increase by 26 chances in 100. In fact, the odds grewby 0.08 per cent. In Australia, where 600,000 women used HRT pre-scare, this would mean 1200 entra cases a year of life-threatening heart attacks, stickes, breast canor and pulmonary embolism, Conversely, abandoning 1977 would lead to 6660 extra cases a *Newel cancer and hip fractures because the therapy

was these numbers are

THE RHOW

2002 News Headlines: CEE + MPA Arm Stopped



WHI History and Context

Estrogen-only HT first came into practice

1960s

Associations shown between HT use and lower rates of CHD, osteoporosis, dementia, and overall mortality in analyses from Nurses Health Study and other observational studies

This resulted in increased prescriptions, making estrogens some of most prescribed medications

1980s, 1990s

WHI estrogen-alone trial stopped early after average follow-up 6.8 years owing to risks outweighing or equaling preventive benefits

2004

Many studies have clarified that the benefit:risk ratio of HT is more favorable in women starting treatment at age <60 or <10 years after menopause onset than in those starting in later menopause. Also, on the basis of mostly observational studies, lower risks of some outcomes have been found for transdermal than for oral estrogens and for micronized progesterone than for medroxyprogesterone acetate

2002-present

1975

Estrogen found to increase risk of endometrial cancer

Adding progestogens for women with uteruses found to protect endometrium and eliminate risk

1993

Women's Health Initiative RCTs and observational studies began

2002

WHI estrogen+progestin trial stopped early after average follow-up 5.2 years owing to risks outweighing preventive benefits

WHI publication followed by 33% decline in estrogen therapy and 66% decline in combined HT in US in first year

HT prescriptions decreased 25-40% in UK and Germany

Today

Few women who would benefit receive HT

Relative Risk vs. Absolute Risk

WHI Findings of Total Cohort Ages 50-79 at enrollment

IAMA | Perious | WOMEN'S HEALTH

The Women's Health Initiative Randomized Trials and Clinical Practice A Review

Johnn E. Marson, MD, DrPH; Carolyn J. Crandall, MD. MS, Jacque E. Rossow, MD. Bewan T. Chibowski, MD, PRD, Garnet L. Anderson, PRD, Marcia L. Stefanic, PRD, Aaron K, Azgaki, MS, Jane A. Cauley, DrPH; Gretchen L. Wells, MD, PhD, Andrea Z. LaCroix, PhD, Cynthia A. Thomson, PhD, RD, Marian L. Neubouse; PhD, Linda Van Hom, PhD, Charles Kopperberg, PhD, Barbara V. Howard, PhD, Leidve F. Tines PhD, Isan Watersack-Mored PhD, Chark S, Purmaier PhD, Prost I, Prestice PhD

		E+P	E alone		
Event	Relative Risk	Absolute Risk (per 10,000 women)	Relative Risk	Absolute Risk (per 10,000 women)	
CHD	1.29*	7 more	0.91	5 fewer	
Stroke	1.41*	8 more	1.39*	12 more	
VTE	2.11*	18 more	1.33	7 more	
Breast CA	1.26	8 more	0.77	7 fewer	
Colorectal CA	0.63*	6 fewer	1.08	1 more	
Hip Fracture	0.66*	5 fewer	0.61*	6 fewer	
Death	0.98	1 less	1.04	3 more	
Global Index	1.15*	19 more	1.01	2 more	



WHI Results by Age for Coronary Heart Disease



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. Oct 02 2013;310(13):1353-68

An Opportunity for Prevention

Hormone Fluctuations

Metabolism, Body Composition, CVD risk

Bone Health and Strength

Energy and Mood

Sleep

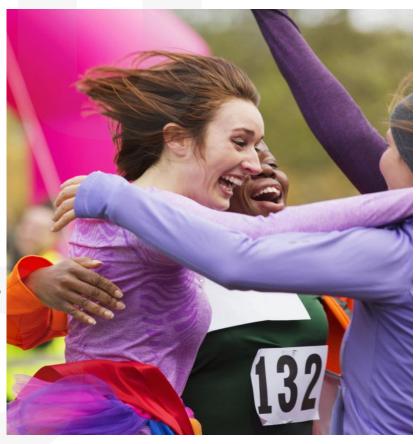
Cognition









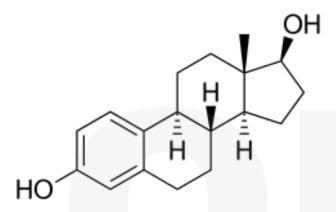


Case 4: What about "Natural Hormones?"

- Same 49 yo patient on CEE and MPA for hormone therapy
- Asks if her therapy is "bio-identical"
- "Should I take supplements?"

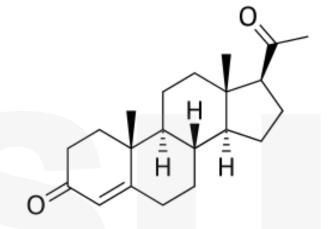






Estrogen

- 4 different human estrogens
 - E1 (estrone), 50-75% weaker than E2
 - E2 (17-beta estradiol)
 - E3 (estriol), placenta, weak
 - E4 (estetrol), fetal in utero
- Conjugated equine estrogen (CEE)
 - 11 active estrogens from pregnant mare urine
 - Premarin brand name
- Synthetics
 - Ethinyl estradiol, estradiol valerate, estropipate
 - Plant derived



Progestogens

- Progesterone only human P
 - Oral not absorbed unless micronized, oil suspension (peanut)
- Synthetic Progestational compounds
 - Medroxyprogesterone acetate
 - Norethindrone, norethindrone acetate
 - Levonorgestrel

FDA Approved *Natural* Hormone Options

Systemic doses of estradiol/progesterone for treatment of hot flashes

- Estradiol oral tablet: Estrace, generics
- Estradiol skin patch: Alora, Climara, Esclim, Menostar, Vivelle (Dot), Estraderm, generics
- Estradiol skin gel/cream: EstroGel, Elestrin, Divigel, Estrasorb
- Estradiol skin spray: Evamist
- Estradiol vaginal ring: Femring
- Progesterone oral tablet: Prometrium, generics
- Estradiol plus progesterone combined oral capsule: Bijuva

Low doses of vaginal estradiol for treatment of vaginal dryness and pain with intercourse

- Vaginal cream: Estrace vaginal cream
- Vaginal ring: Estring
- Vaginal tablet: Vagifem
- Vaginal insert: Imvexxy



Case 5: Bleeding on HT

- 56 yo, started Combipatch four months ago for severe vasomotor symptoms.
- Final menstrual period at 55 yo.
- Reports episodic spotting every few days.
- Now what?



Bleeding with Hormone Therapy



Timing

Common within first 6 months, particularly if recently menopausal

Or with dose adjustments or missed doses

Red flags: heavy, worsening bleeding

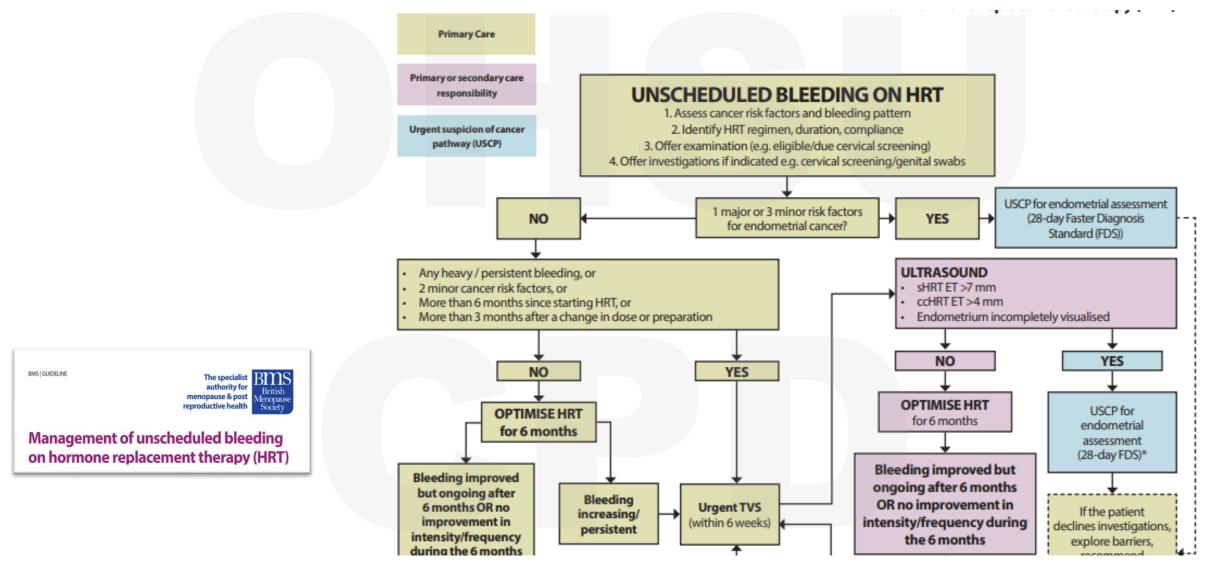
Consider endometrial cancer risk factors



Imaging

Transvaginal ultrasound first step

Tip 3: Work-up for Bleeding on HT



A Few Evidence-based Medicine Tips

Which would you choose?

- 99.9% chance of winning \$100, p=.001
- 95% chance of winning \$10,000, p = .05

Both statistically significant but one is more relevant



50 years old in 2020





Case 6: To Stop or Continue Hormones?

- 70-year-old patient on HT since her mid 50s
 - Hysterectomy in late 40s for heavy bleeding due to fibroids
 - Vivelle dot estradiol patch 0.0375mcg
- Patient message refill request for patch "keeps my skin young"
 - Has never tried to taper
 - Up to date on breast and colon ca screening



Ongoing Risk Assessment and Shared-Decision Making

Dexa scan

Counseling on role of HT on breast cancer risk (E+P more so)

VTE risk discussion

CVD risk assessment

Tip 4: Risk stratification



Table 6. Atherosclerotic Cardiovascular Disease Risk Score and Years Since Menopause Onset for Initiating HT

Cardiovascular disease risk over 10 years	Years since menopause onset				
American College of Cardiology/Ameri- can Heart Association atherosclerotic cardiovascular disease risk score	≤5	6-10	≥10		
Low risk (<5%)	HT acceptable	HT acceptable	Consider alternatives; HT acceptable with individualized, shared decision-making		
Intermediate risk (≥5.0% to <10%)	HT acceptable. Consider transdermal HT depending on risk factors	HT acceptable. Consider transdermal HT depending on risk factors	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making		
High risk (≥10%)	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Generally advised to avoid systemic HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making	Avoid HT. Consider alternative therapy, and if severe VMS persist, individualized, shared decision-making		

HT indicates hormone therapy; and VMS, vasomotor symptoms.

Questions?

