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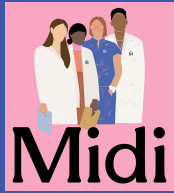
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Managing Menopause Symptoms in Cancer Survivors



MidiHealth



Topics to review:

Menopause Overview

Why Cancer Treatments impact Menopause

Management Options for Hot Flashes

Management Options for Genitourinary Syndrome of Menopause

Hormone Therapy in those At Risk and in Cancer Survivors

Testosterone in Cancer Survivors

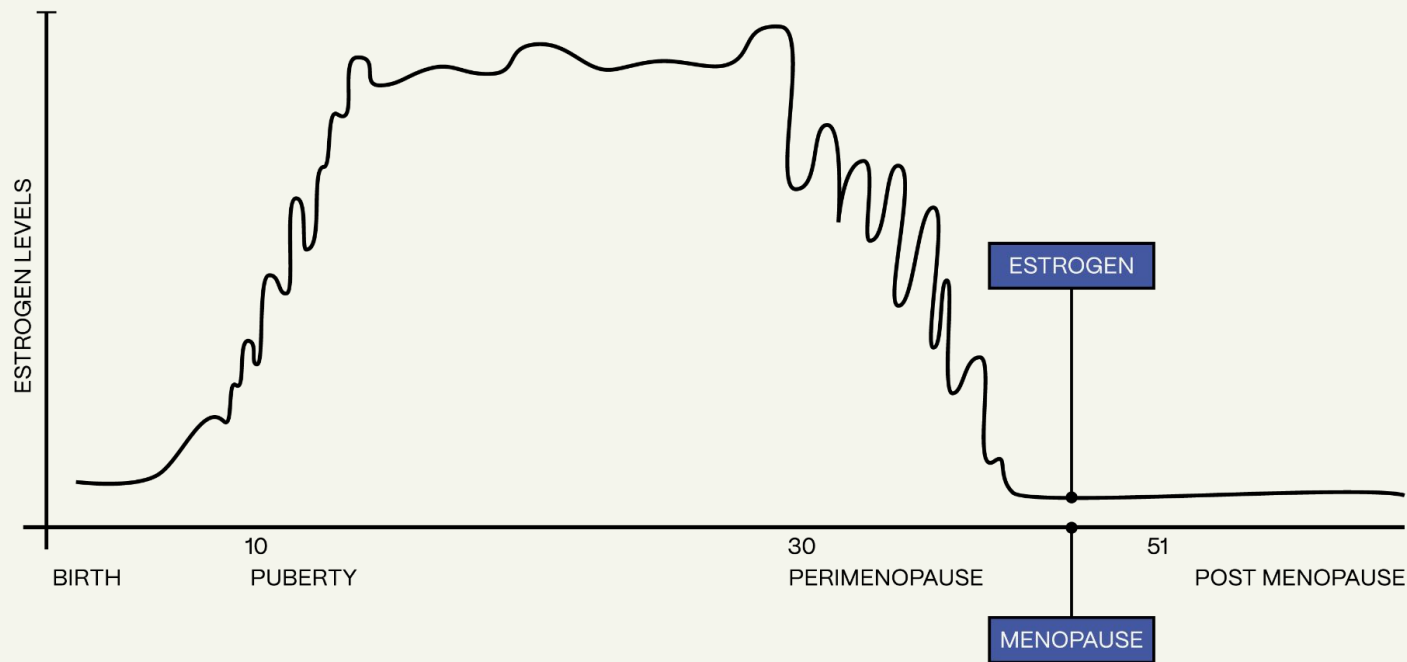


Menopause and Perimenopause Definitions



- Menopause- defined by 1 year without a menses
 - Average age in the US is 51
 - Doesn't apply to those with a progestin IUD, those on Tamoxifen
- Perimenopause- the months or years preceding menopause during which time cycles can change but women can experience the same symptomatology
 - Average length 4-6 years but can go on as long as 14 years

How estrogen levels shift over time

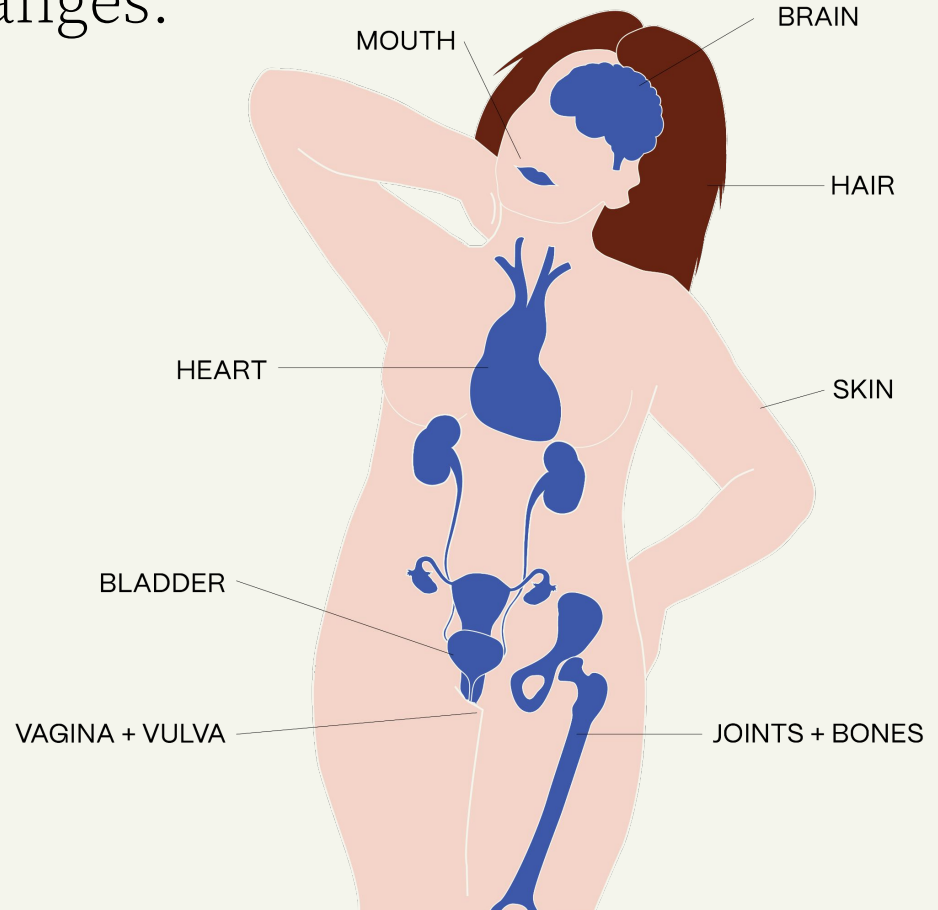


Where you might feel the changes:

Estrogen receptors are everywhere

Estrogen supports nearly every organ
and system in the body

“Estrogen withdrawal” is real



Menopause Symptoms

Hot flashes

Anxiety/Depression

Urinary urgency

Dry mouth

Night sweats

Vaginal dryness

Stress incontinence

Joint pain

Sleep trouble/Insomnia

Painful intercourse

Recurrent UTIs

Irregular heartbeat

Brain fog/Memory lapses

Difficulty achieving
orgasm

Hair and skin
changes

Changes in bowel function

Mood changes

Decreased libido

Itchy skin

And many more!

Irritability

Weight gain

85% of women have at least 1 or more of these symptoms

Why do some cancer therapies bring on early menopause?

CHEMOTHERAPY

- Damages ovarian follicles, sometimes permanently
- Women over 40 are more likely to have permanent menopause

RADIATION

- Pelvic radiation can impact ovarian function

SURGICAL MENOPAUSE

- Some treatments may involve ovarian removal with immediate onset of surgical menopause

ENDOCRINE THERAPIES

- Some endocrine therapies like Aromatase Inhibitors require ovarian shutdown for effectiveness

Less data with newer targeted and immunotherapies

Because of the abrupt onset of induced menopause symptoms are sometimes more severe in cancer survivors.

Why do some cancer therapies cause menopause symptoms?



Endocrine (Hormonal) Therapies

Some breast cancer treatments include tamoxifen, which may impact menstrual cycles and cause hot flashes and night sweats

Some breast cancer treatments include aromatase inhibitors which can cause hot flashes and severe vaginal dryness symptoms





Management of Hot Flashes and Night Sweats- Non Hormonal Options

- Lifestyle Options - ok for ALL!
- Low dose antidepressants – Venlafaxine, paroxetine, fluoxetine, citalopram, escitalopram, desvenlafaxine, mirtazapine, sertraline
- Anticonvulsants - Gabapentin and Pregabalin
- Anticholinergics/antimuscarinics- Oxybutynin
- FDA Approved Options:
 - Fezolinetant (Veoza)
 - Elinzanetant (Lynkuet)
 - Low dose Paroxetine (Brisdelle)
- Integrative options- CBT, mindfulness, acupuncture, relaxation therapies
- Herbs and botanicals



Deeper Dive on Prescription Alternatives



- Doses of many of these drugs are typically lower than what the drug is intended for
 - For off label drugs all felt to be effective although no real head-to-head comparisons
 - For antidepressants beneficial effect in days not weeks
 - Take advantage of the drug side effects - sedation with Gabapentin, less urinary urgency/frequency with Oxybutynin
- Generally try not to mix and match
- Paroxetine often avoided for women on tamoxifen as blocks the conversion of tamoxifen to its active metabolites through CYP2D6 part of the liver detoxification pathway
- The newer drugs Fezolinetant (Veoza) and Elinzanetant (Lynkuet) are the first drugs that we understand the exact mechanism of action
 - Targets the neurokinin receptors which lowers KNDY neuron signaling
 - Lynkuet targets NK1/NK3 and may also help with sleep
- Generally wean these drugs when discontinuing

Main Point:

NO ONE NEEDS TO SUFFER!!





Genitourinary Syndrome of Menopause (GSM)

- Genitourinary syndrome of menopause (GSM) is a collection of signs and symptoms caused by decreased estrogen levels that affects vagina, vulva and lower urinary tract
- It can cause vaginal dryness, burning, and painful intercourse, as well as urinary urgency, burning, and frequent infections
- GSM is a progressive condition that can impact a woman's physical, emotional, and sexual health

Why Do Cancer Survivors Experience So Much GSM Symptoms?

- Treatment Induced Menopause
- Radiation Effects on the Vaginal Tissue
- Side Effects of Medications like Aromatase Inhibitors
 - These drug function by shutting down all estrogen production in the body (beyond just the ovaries) such that women are “more shut down” than menopause
 - Can get pain with sitting, tearing of the tissue- can feel like “sand paper”
 - Normally, no one “thinks about their vagina” – but if women want to use it, they have to think about it!

How to Treat Vaginal Dryness in Breast Cancer Survivors

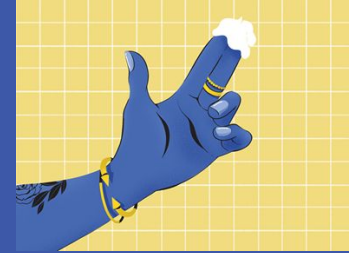
Over the Counter Options:

- Vaginal Moisturizers – retain water and provide longer term relief – many different types with different products in them
- Oils- penetrate thin tissue and soothing and can be used both internally and externally - “coconut oil suppositories”
- pH balanced agents with Hyaluronic acid
- Soothing agents for vaginal or vulvar pain
- Topical anesthetics for introital discomfort
- Lubricants for sexual activity



What About Vaginal Estrogen?

- Benefits of local vaginal hormones
 - Targeted efficacy to vaginal tissues
 - Minimal systemic absorption, fewer adverse effects
 - Comes in different ways- creams, rings, suppositories
 - Intravaginal creams tend to be avoided for women on aromatase inhibitors but can be safely rubbed into the vaginal opening or along the outside
-
- No evidence that impacts breast cancer survival



Review > Am J Obstet Gynecol. 2025 Mar;232(3):262-270.e1. doi: 10.1016/j.ajog.2024.10.054.
Epub 2024 Nov 7.

Vaginal estrogen use in breast cancer survivors: a systematic review and meta-analysis of recurrence and mortality risks

Mary E Beste ¹, Andrew M Kaunitz ², Jordan A McKinney ², Luis Sanchez-Ramos ³

Affiliations + expand

PMID: 39521301 DOI: 10.1016/j.ajog.2024.10.054

What About Lasers and Energy Devices To Treat GSM



- Includes micro ablative CO2 laser – “Mona Lisa” and non-ablative “Yag”
- Also energy-based devices - FemLift, Fem Touch, vFit, ThermiVa, diVa, vSculpt
 - Each work differently but essentially cause microtrauma to the tissue causing new blood supply, collagen production to promote tissue healing
 - None are FDA approved for these indications
 - Large out of pocket costs - not covered by insurance
 - Done by some gynecologists, dermatologists or plastic surgeons
 - For lasers, FDA put out warning statements for the potential for burns (not seen in studies)
 - Many studies have been done, different settings and endpoints
 - **Overall felt to improve symptoms of GSM**

Hormone Therapy in Cancer Survivors



Systemic Hormone Therapy



- Includes Estrogen with or without Progesterone
 - Estrogen alone used if hysterectomy has been done
 - Comes in transdermal forms (patches, sprays, gels), oral, or vaginal rings
- The most effective treatment for managing symptoms with symptom relief in days
- Unless other health contraindications can be used in those with non hormonal cancers, and most gynecologic cancers (including early stage endometrial and most ovarian cancers)
- Main controversies have been in breast cancer

Systemic Hormone Therapy - General Information

- Timing hypothesis- if started within 10 years of LMP:
 - Will treat symptoms and also is protective for heart disease, bone loss, likely cognitive loss and all cause mortality

- Can be used in the perimenopause
 - Will not provide contraception
 - If heavy or abnormal bleeding a symptom of perimenopause oral contraceptives or progestin IUD recommended because menopausal hormone therapy won't control bleeding

Hormone Therapy and Breast Cancer - What Do We Know?

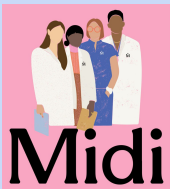


- The “Gold Standard Study” was the WHI which showed a specific formulation of MHT - oral conjugated estrogen and synthetic progestin increased risk of breast cancer after approx 5 years of use compared to placebo
- The WHI also showed that for women who took estrogen alone (post hysterectomy) there was a lower risk of breast cancer compared to placebo, and long term follow up showed that that oral estrogen alone was associated with a **statistically lower risk of getting or dying of breast cancer**
- Current formulations of menopausal hormone therapy use bioidentical progesterone which is thought to be more breast neutral and the studies showing increased breast risk is largely based on studies with synthetic progestins
- There is mixed results looking at whether the use of hormone therapy increases risk of recurrence in women with prior breast cancer but these studies have mainly looked at older formulations of hormones
- There is a lack of data looking at current formulations of hormone therapy in women with prior breast cancer

Not All Hormone Therapy is the Same

- Duavee - combines and oral estrogen with bazedoxiphen, a cousin drug of Tamoxifen
- Bazedoxifene has been shown to protect the lining of the uterus from uterine cancer
- It is being studied for prevention of breast cancer in high risk women (those with breast atypia or DCIS)





Hormone Therapy After Breast Atypia and DCIS

- First line recommendations should be non-hormonal options
- Off label use of Duavee if late perimenopausal or menopausal
- Standard menopausal hormone therapy ok in the setting of DCIS and bilateral mastectomies
 - Risk of getting invasive breast cancer 1-2% over lifetime
- Shared decision making for standard MHT for all breast atypia and DCIS with remaining breast tissue



Hormone Therapy with Invasive Breast Cancer - Is it Safe?

Hormone Negative Breast Cancer

- No data that the use of menopausal hormone therapy increases risk of recurrence in hormone negative disease
- Typically not recommended in first 2 years given highest risks of recurrence
- Between years 3-5 would offer in conjunction with breast oncology
- After 5 years considered “cured” and would freely offer





Hormone Therapy with Invasive Breast Cancer - Is it Safe?

Hormone Positive Breast Cancer

- Non-hormonal options should always be first line
- Data looking at use of hormone therapy post breast cancer has shown mixed results and lack of studies looking at current formulations of bioidentical hormones in those with breast cancer
- Generally avoid in first 5 years as most people will be on adjuvant endocrine therapy (ie Tamoxifen)
- Even though can see late recurrences (15-20 years) in those with early stage disease can do shared decision making after 5 years
- If giving hormone therapy can do off-label Duavee (no studies in invasive cancer) or standard menopausal hormone therapy

Testosterone in Cancer Survivors

- The vaginal and vulva and urinary tract are rich with androgen receptors
- Best evidence for testosterone is for improving libido in postmenopausal women
- Evolving evidence in:
 - Bone loss/osteopenia/osteoporosis
 - Muscle mass/body composition
 - “Brain fog”/cognition
 - Overall wellbeing
 - No clear data that should be a part of menopausal hormone therapy
- Less evidence in cancer survivors Particularly those with breast cancer on aromatase inhibitors



Other Options for Improving Sex Drive in Survivors

Flibanserin (Addyi)- novel non-hormonal, multifunctional serotonin agonist antagonist (MSAA)

- Increases dopamine and norepinephrine (both responsible for sexual excitement) while decreasing serotonin (responsible for sexual satiety/inhibition).
- FDA approved in 2015 to treat Hypoactive sexual desire disorder (HSDD) in premenopausal women
- Off label- use for postmenopausal women (obtain from specialized pharmacies)
Almost no data in cancer survivors - small trial presented at ASCO 2023 looked at 37 breast cancer survivors on adjuvant endocrine therapy and showed improvements in multiple domains of sexual functioning
- Although limited data in survivors not a contraindication in hormone positive cancers

Other Options for Improving Sex Drive in Survivors

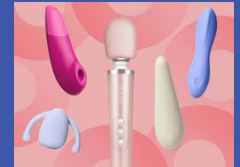
Bremelanotide (Vyleesi) – peptide agonist of melanocortin receptors that acts to reduce inhibitor and increase excitement

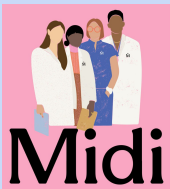
- FDA approved in 2019 for hypoactive sexual desire disorder (HSDD) in premenopausal women
- Off-label use for postmenopausal women (need to obtain from specialized pharmacies)
- Preclinical data suggest possible antitumor effects in glioblastoma cell lines
- No published data in cancer survivors
- Although no data in breast cancer survivors not contraindicated based on mechanism of action (NCCN says to individualize)



Remember Supportive Services to Help Manage GSM and Sexual Dysfunction

- Pelvic Floor Physical Therapy
- Vaginal Dilators
- Devices like Ohnut Rings
- Sex Therapies (AASECT - The American Association of Sexuality Educators, Counselors and Therapists)
- Vibrators for Pleasure





Common Questions?

Do hormones need to be stopped at a specific age - **NO**

Can hormones be used if there is a family history of breast cancer - **YES**

Can hormones be used if someone has a genetic mutation like the BRCA genes that increase the risk of breast cancer - **YES**

Can supplements, herbs, botanicals be used with cancer therapies - **MAYBE**

THANK YOU!



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