

Women's Mood Disorders Across The Lifespan

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Assistant Professor

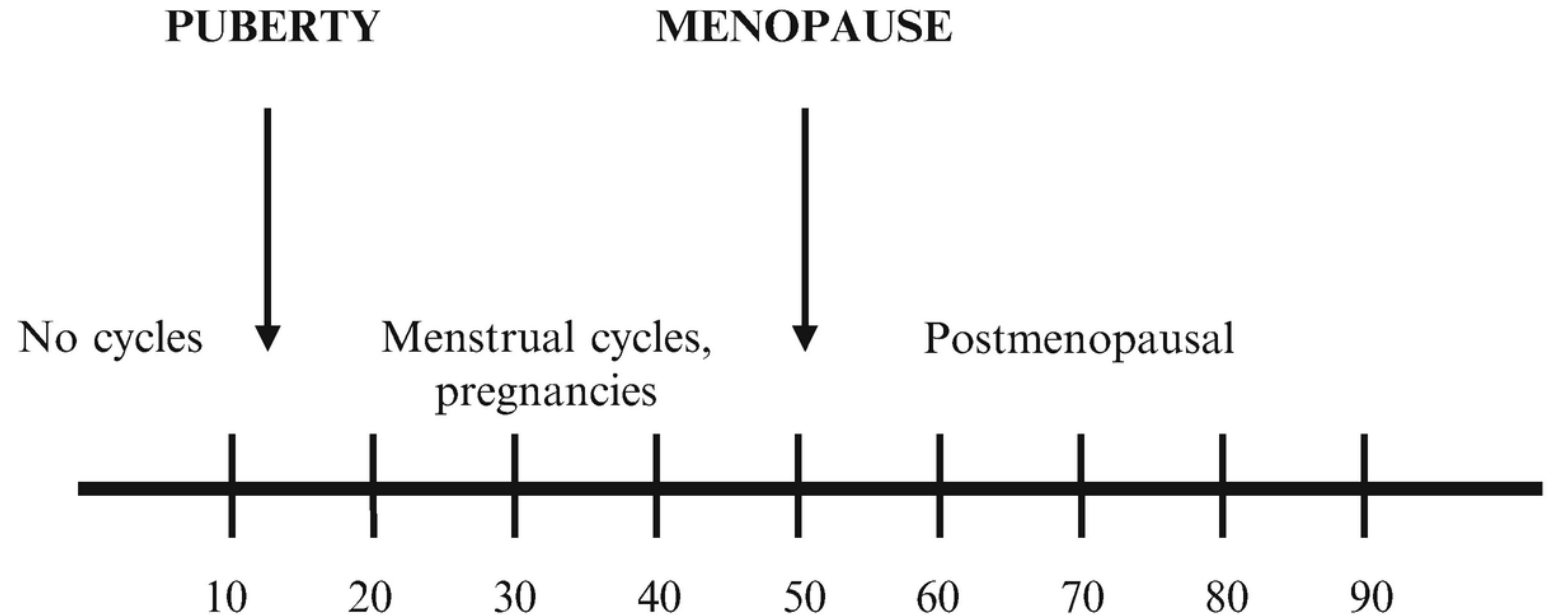
UNC Center for Women's Mood Disorders Center

I have no disclosures

Objectives

To discuss the epidemiology, clinical presentation, and general approach to the management of perimenstrual and perimenopausal disorders

FEMALE LIFESPAN



The Increased Risk for Depression in Women Begins at Puberty

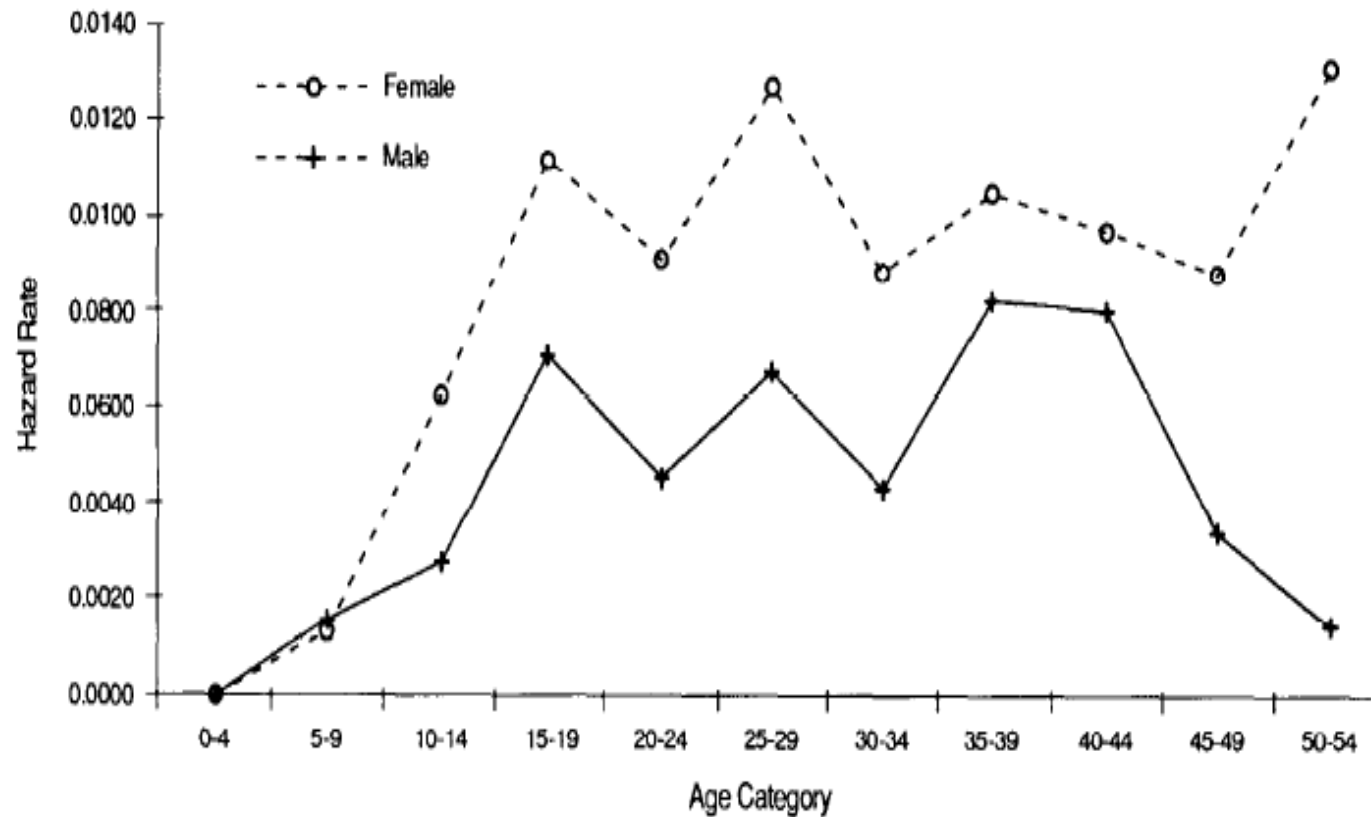
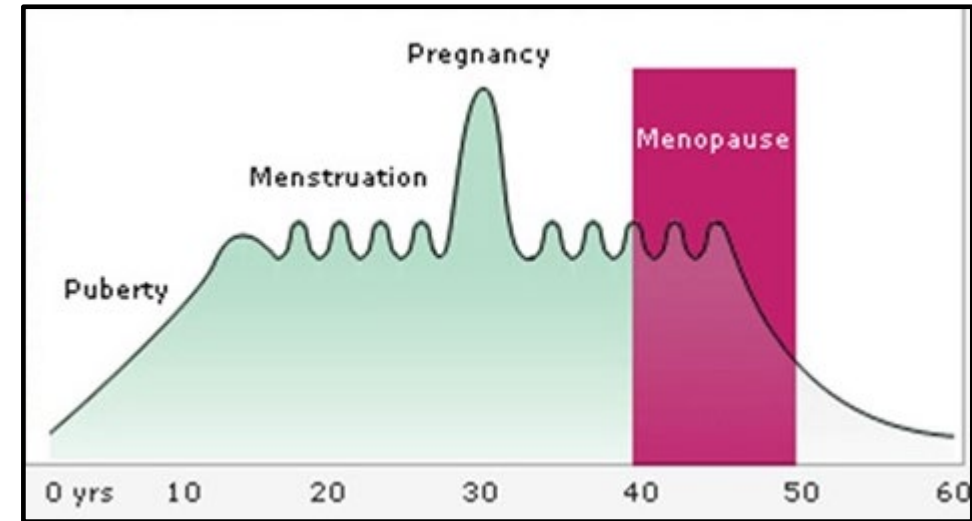


Fig. 1. MDE hazard rates by age and sex.

A subset of women have mood symptoms associated with reproductive transitions

Fluctuations in gonadal steroids are a part of normal reproductive events

Some women are more **sensitive** to these normal hormonal shifts

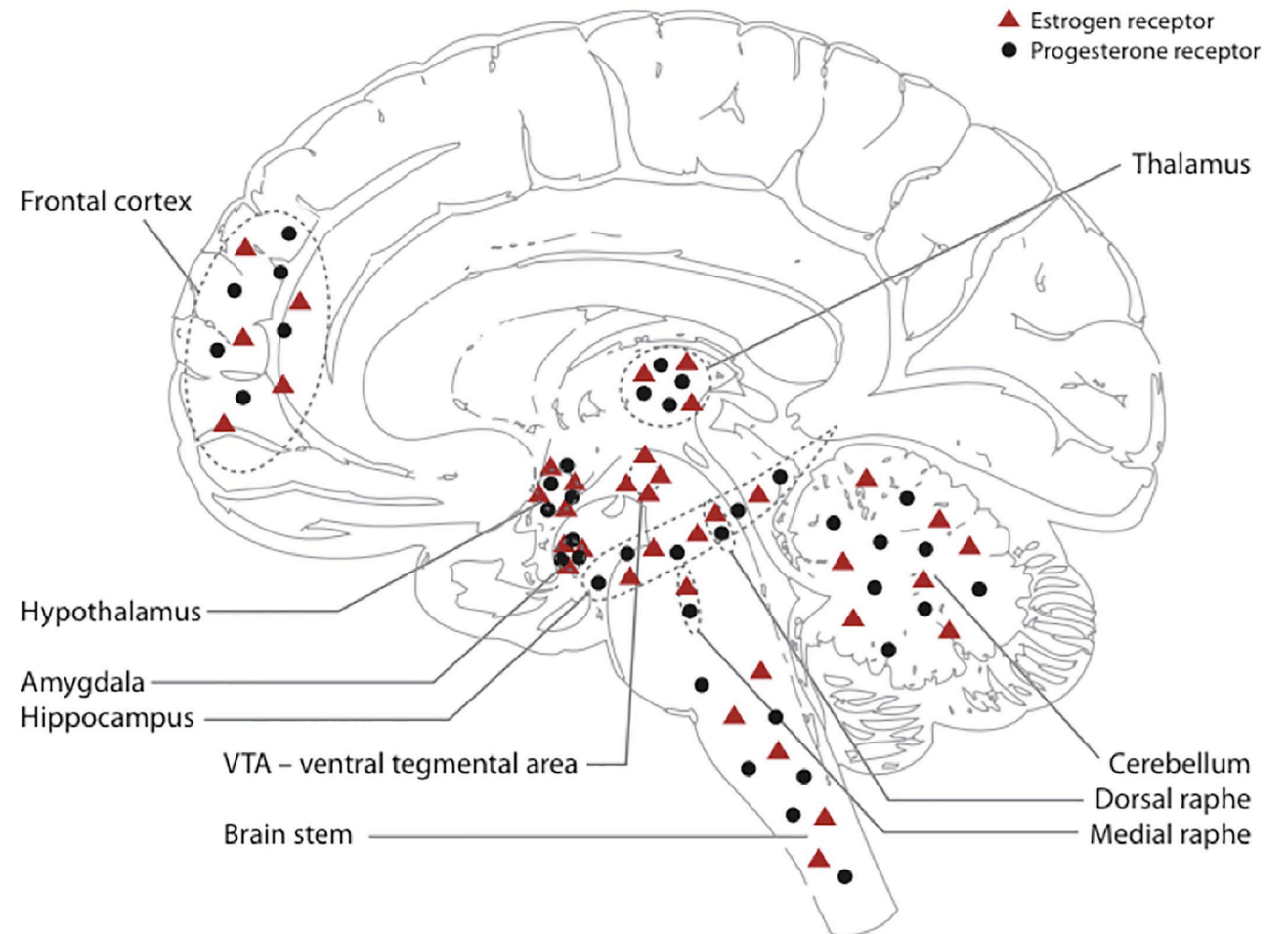


Gonadal steroid hormones impact neurotransmitter pathways and structural brain regions

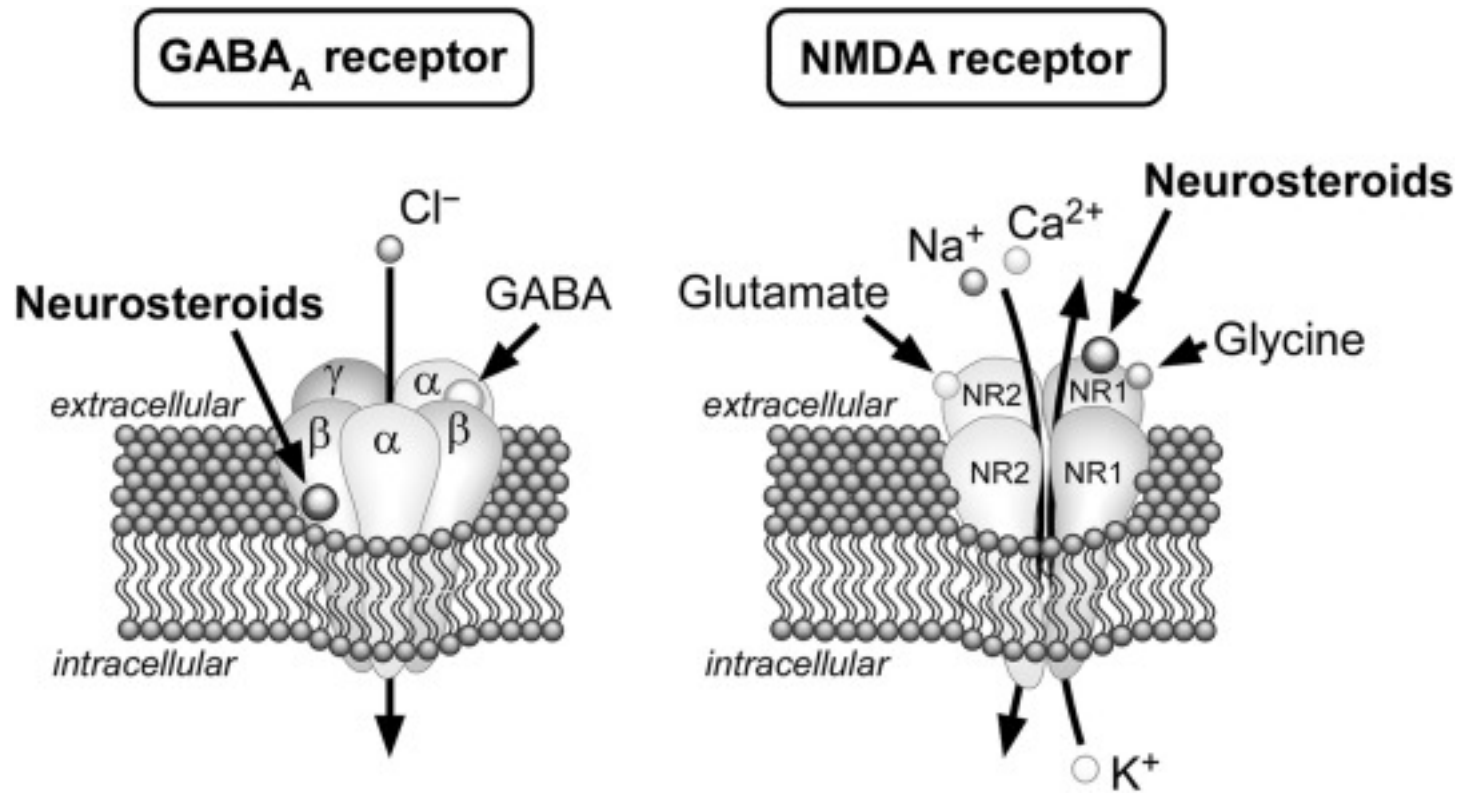
Progesterone acts on GABA-A receptor complex

Estradiol may act on serotonin transporter

Estrogen receptors are present on brain structures linked to emotion processing



Role of neuroactive steroids: allopregnanolone



Taking a reproductive history is currently the best method of assessing risk

- **Family history of reproductive exacerbations**
- **Personal history of mood symptoms during reproductive transitions**
- **Sensitivity during changes in hormonal medications**
- **Exposure to early life stressors/trauma**

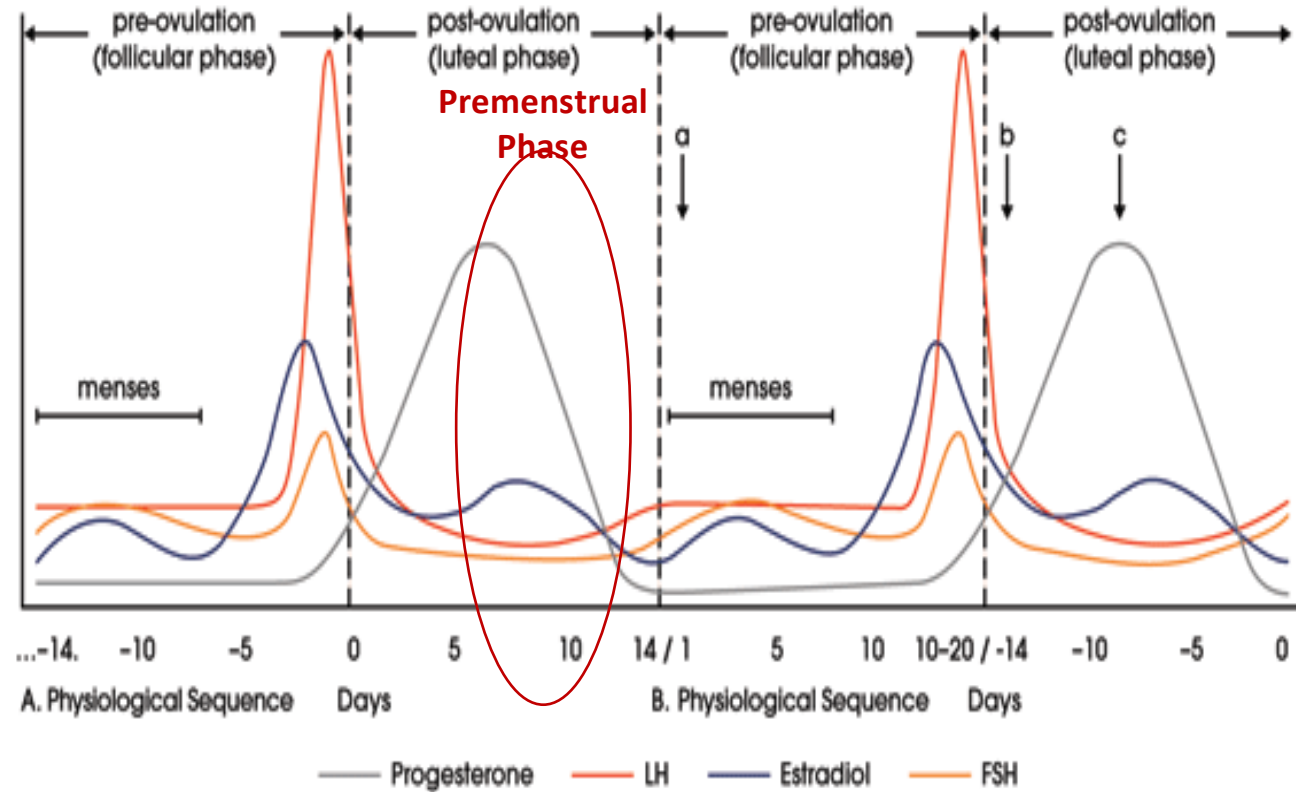


Menstrual disorders

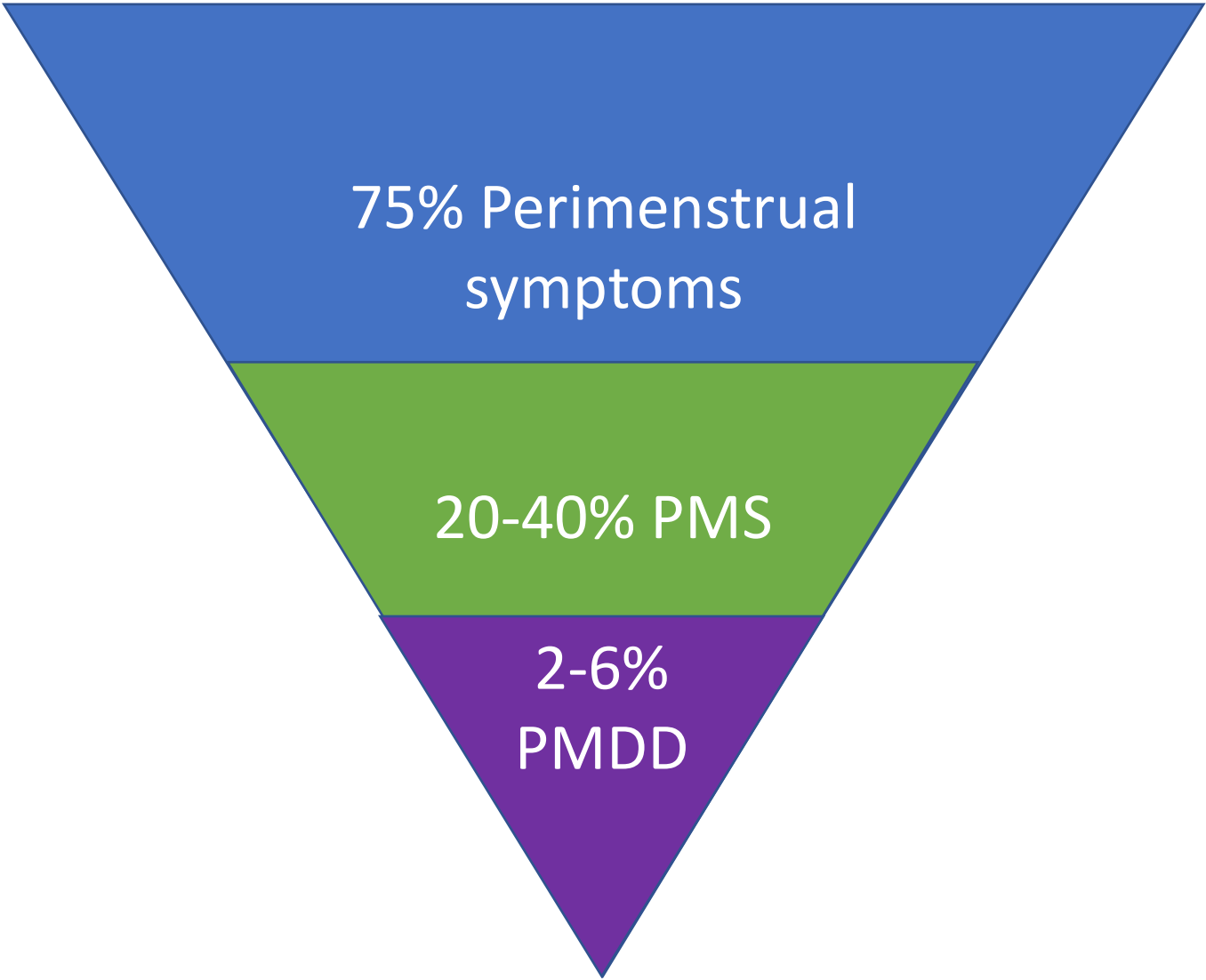


Menstrual Cycle

Figure
The "Normal" Pattern of Hormonal Changes that Regulate the Ovarian Cycles



a=gonadotropin-releasing hormone analogues, continuous psychotropics; b=intermittent psychotropics, possible progesterone antagonists, possible progestin antagonists; c=Possible symptomatic interventions (eg, anxiolytics); LH=luteinizing hormone; FSH=follicle-stimulating hormone.



Premenstrual Syndrome

Not listed in DSM-5

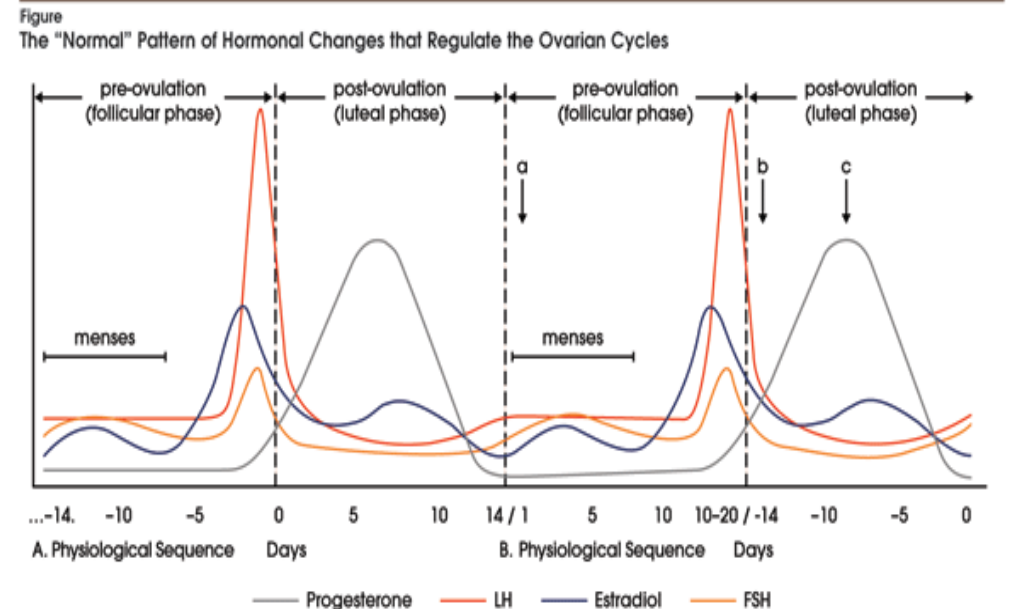
ACOG definition of PMS:

At least 1 symptom associated with economic or social dysfunction

Occurs during the 5 days before onset of menses and is present at least 3 consecutive menstrual cycles

Symptoms may be affective or physical

Impacts 20-40% of women



a=gonadotropin-releasing hormone analogues, continuous psychotropics; b=intermittent psychotropics, possible progesterone antagonists, possible progestin antagonists; c=Possible symptomatic interventions (eg, anxiolytics); LH=luteinizing hormone; FSH=follicle-stimulating hormone.

Halbreich U, Monacelli E. *Primary Psychiatry*. Vol 11, No 12. 2004.

Premenstrual Dysphoric Disorder (PMDD)

Timing of symptoms is central

Combination of somatic symptoms and severe mood symptoms

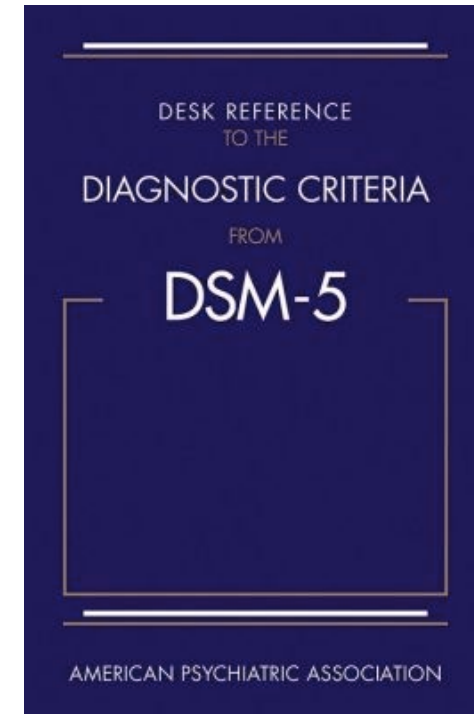
Clinically significant distress or impairment

MUST be confirmed prospectively

Prevalence estimates range from 2% to 6% of menstruating women

Association with seasonal affective symptoms

Differential: rule-out mood disorder with premenstrual exacerbation



Tracking Symptoms is Key to making the diagnosis

Premenstrual Mood Chart

Name _____
 Doctor _____ Year _____

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Jan																															
Feb																															
Mar																															
April																															
May																															
June																															
July																															
Aug																															
Sept																															
Oct																															
Nov																															
Dec																															

= menstrual flow

Rating scale for mood/depression, irritability, anxiety, other _____
 1 = good
 2 = ok
 3 = poor
 4 = terrible

Examples:

#1 probable PMS

1	2	3	4	4	4	2	1	1	2
---	---	---	---	---	---	---	---	---	---

#2 probable depression

2	3	4	3	3	4	3	3	4	2
---	---	---	---	---	---	---	---	---	---

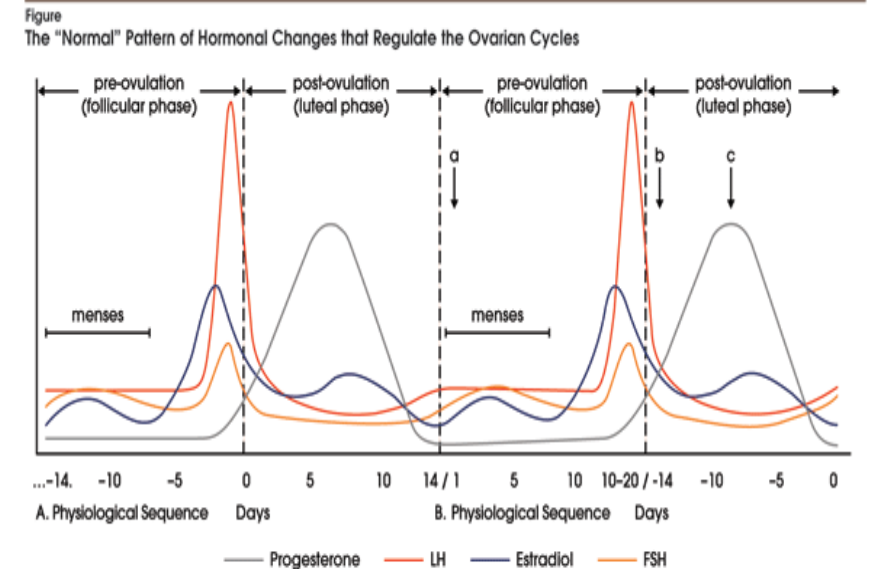
Daily symptom monitoring across 2 cycles

Role of Hormones in PMDD

No evidence of menstrual hormone irregularity or disturbance

Reproductive hormones may trigger mood dysregulation in the context of an antecedent susceptibility

Checking hormones levels is not currently recommended!



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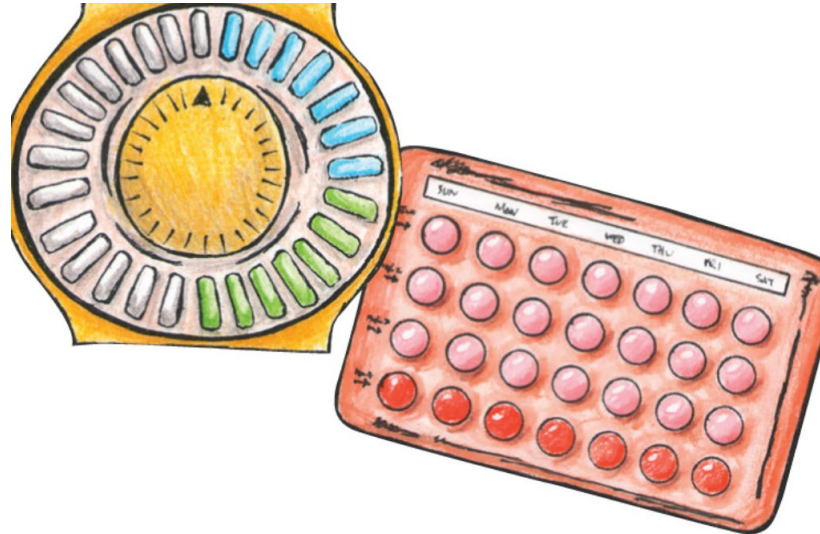
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Menstrual Disorder Treatment Options

Psychiatric Medications

Hormonal Treatments

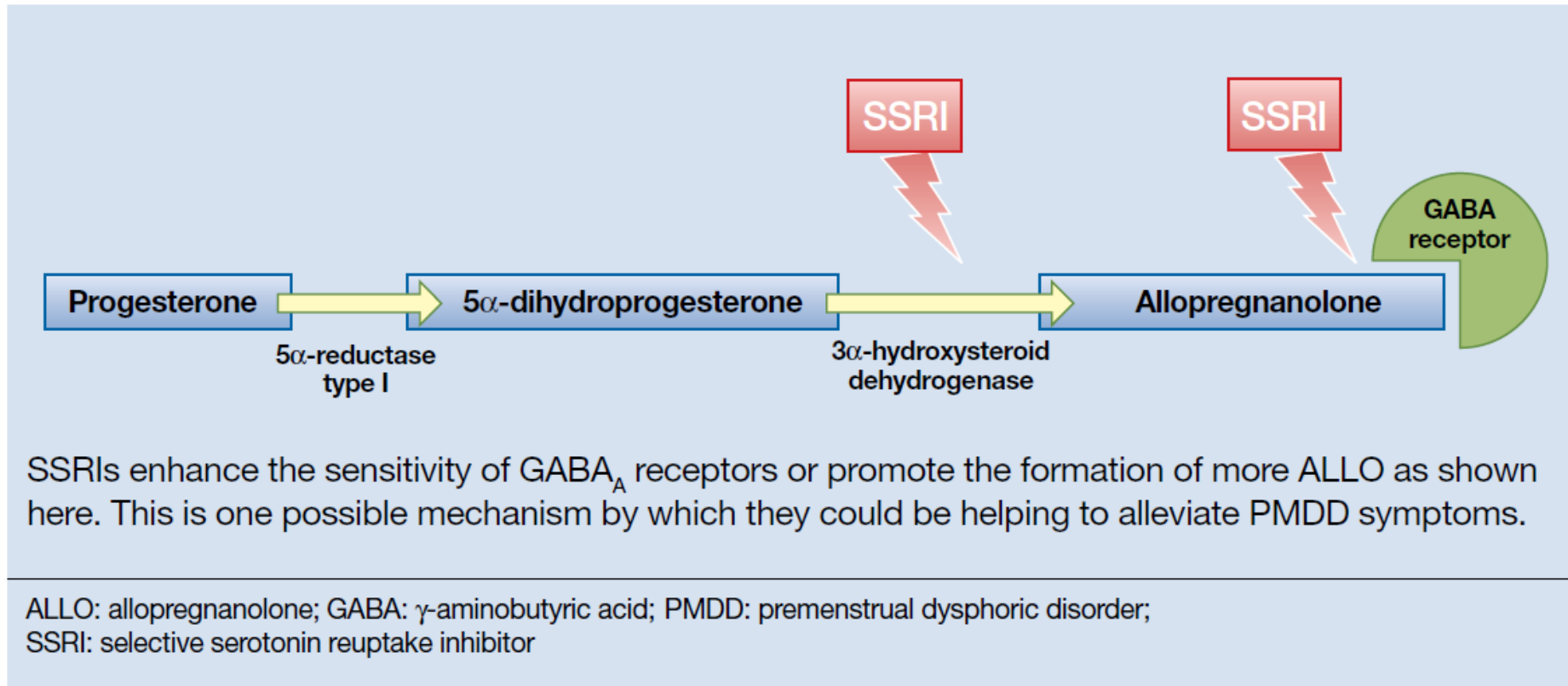
Supplements/Behavioral
Modification



Why serotonergic antidepressants?

Figure 4

Conversion of progesterone to ALLO and the SSRI influence



Menopause



Common Menopausal Symptoms

**Study of Women's Health Across
the Nation**

**Seattle midlife Women's Health
Study**

Penn Ovarian Aging Study POAS

MsFLASH



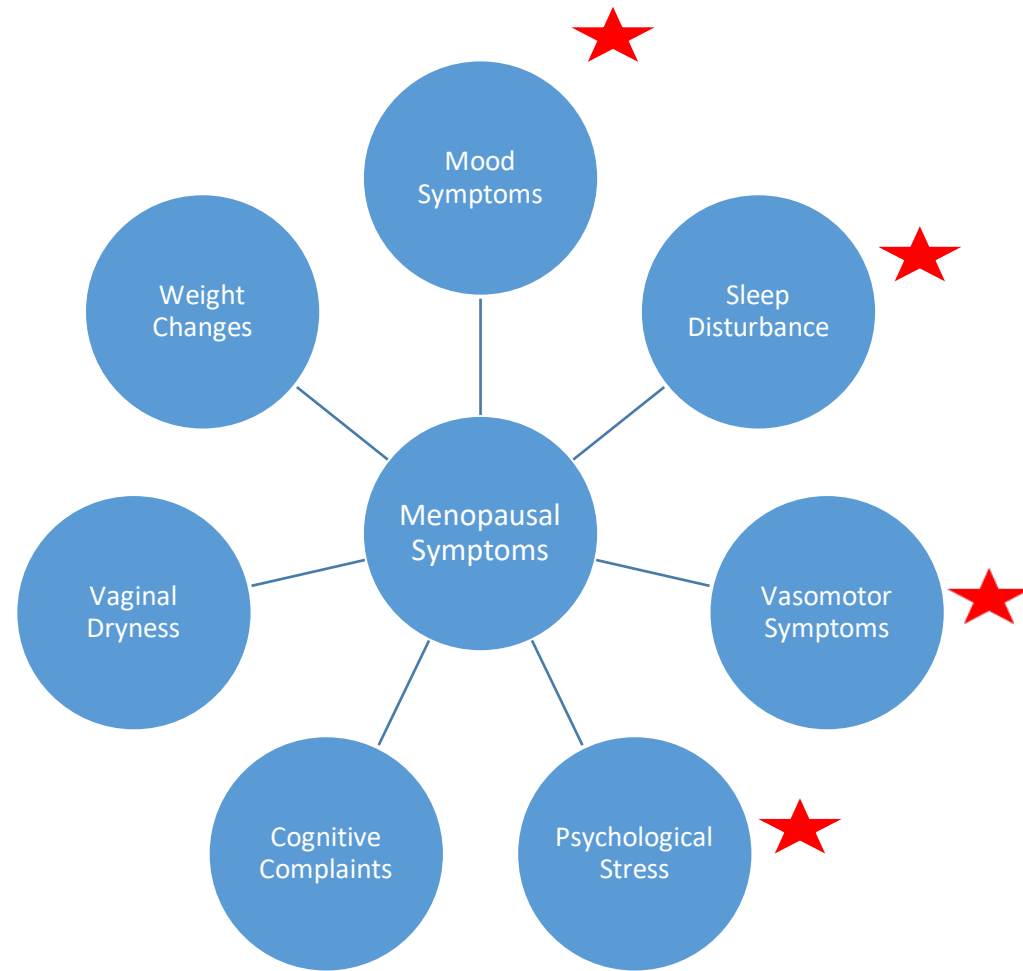
Common Menopausal Symptoms

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MsFLASH



Depressive symptoms are common during perimenopause

'sub-syndromal' symptoms most common

Women at highest risk for a MDE have a history of MDD

First lifetime MDE during the menopausal transition is less common

Independent of estradiol level



Differential

The differential for mood symptoms during the menopausal transition should include:

- Affective Disorders
- Psychological distress
- Bereavement
- Adjustment disorder
- Other medical etiologies
- Anxiety

Previously the '*domino theory*' was the prevailing theory for depression during perimenopause

Vasomotor symptoms (VMS)



Sleep Disturbance



Depression

Severe VMS are not necessarily associated with depressive sx

Night VMS linked w/ depressive sx independent of sleep disturbance

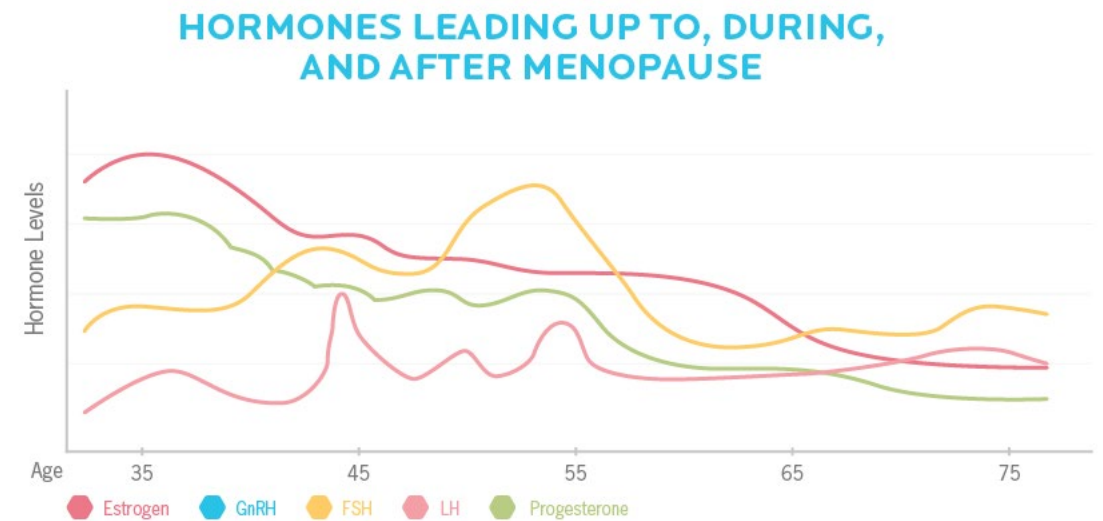
Pathophysiology

Greater variability in estradiol levels

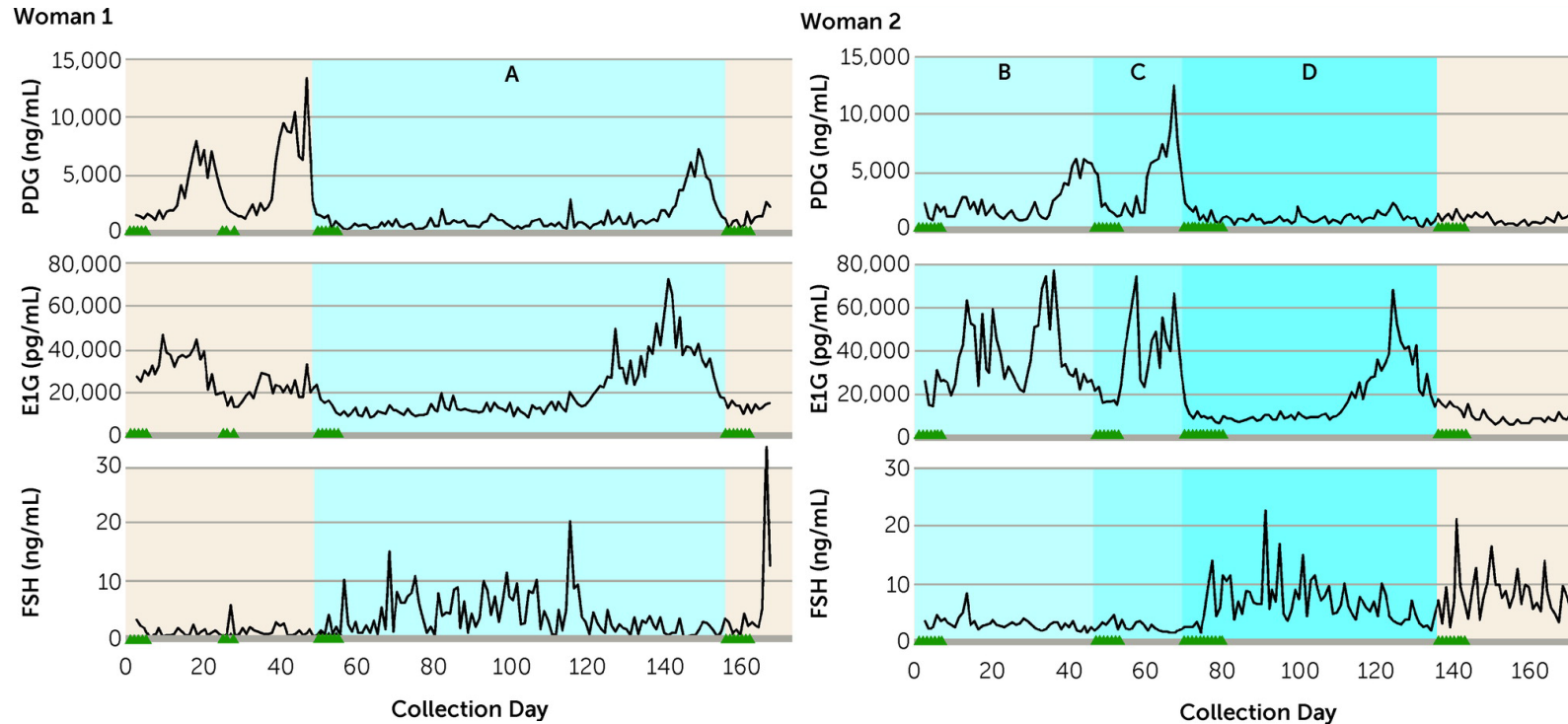
May impact neurotransmitters involved in the pathophysiology of affective exacerbations and neuronal architecture

Allopregnanolone fluctuations implicated

Hypothalamic-Adrenal-Pituitary (HPA) axis interactions

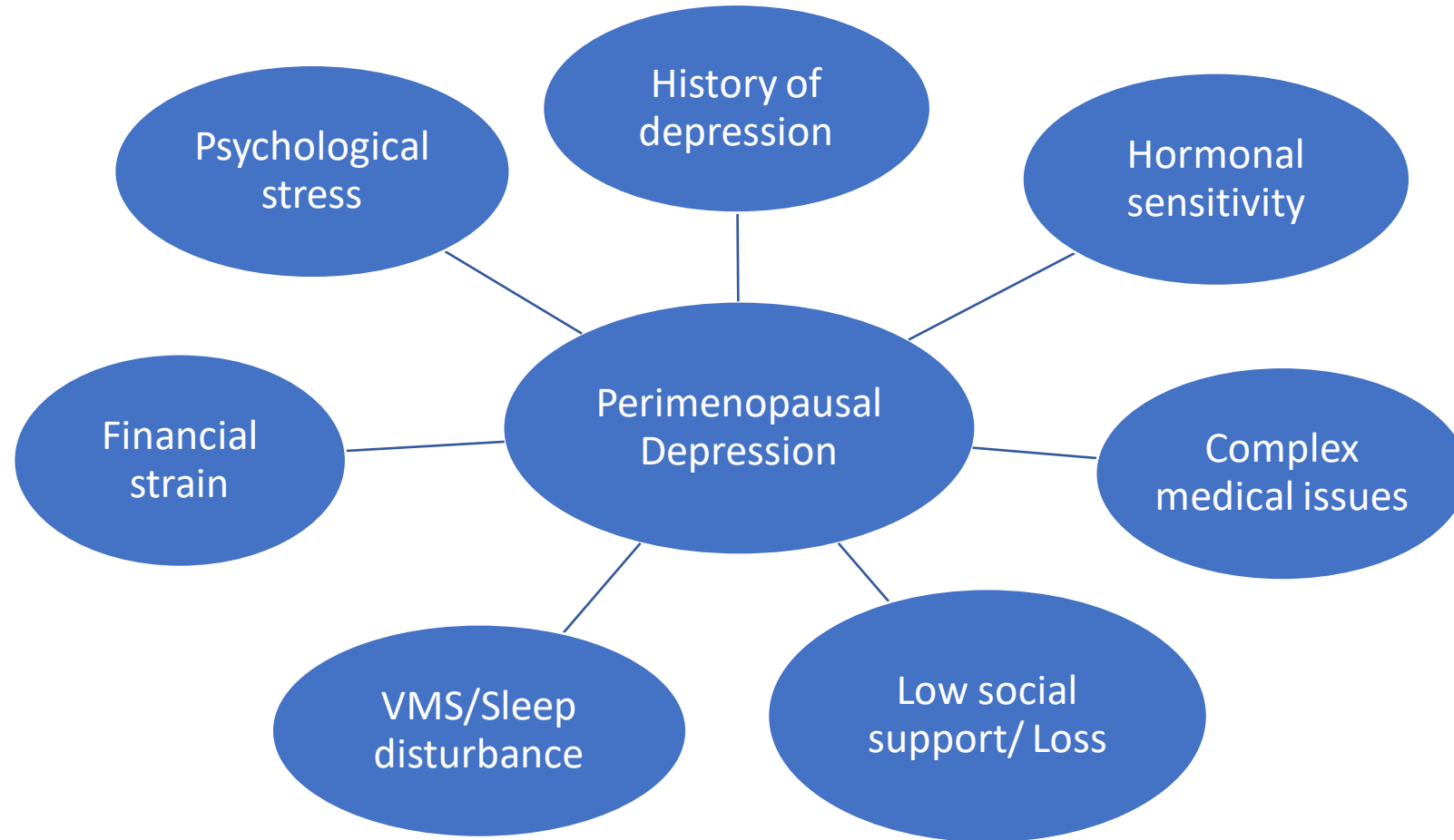


Sex steroid levels are highly variable during the perimenopause



b A, a long ovulatory cycle; B, a long ovulatory cycle with low luteal progesterone; C, a normal ovulatory cycle; and D, a long anovulatory cycle. Triangles on the x-axis represent days of menstrual bleeding. PDG, pregnanediol-glucuronide; E1G, estrone-glucuronide; FSH, follicle-stimulating hormone.

Who is most likely to develop symptoms?



Available screening scales can be helpful

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ DATE: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(use ~ to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3

add columns + +

TOTAL:

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card).

Which of the following symptoms apply to you at this time?
(X ONE Box For EACH Symptom) For Symptoms That Do Not Apply, Please Mark "None".

Symptoms:

	none	mild	moderate	severe	extremely severe
Score =	0	1	2	3	4
1. Hot flashes, sweating (episodes of sweating).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Irritability (feeling nervous, inner tension, feeling aggressive)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Anxiety (inner restlessness, feeling panicky)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Sexual problems (change in sexual desire, in sexual activity and satisfaction).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Joint and muscular discomfort (pain in the joints, rheumatoid complaints)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Spectrum of symptoms in perimenopausal depression

Depressed mood

Irritability

Anhedonia

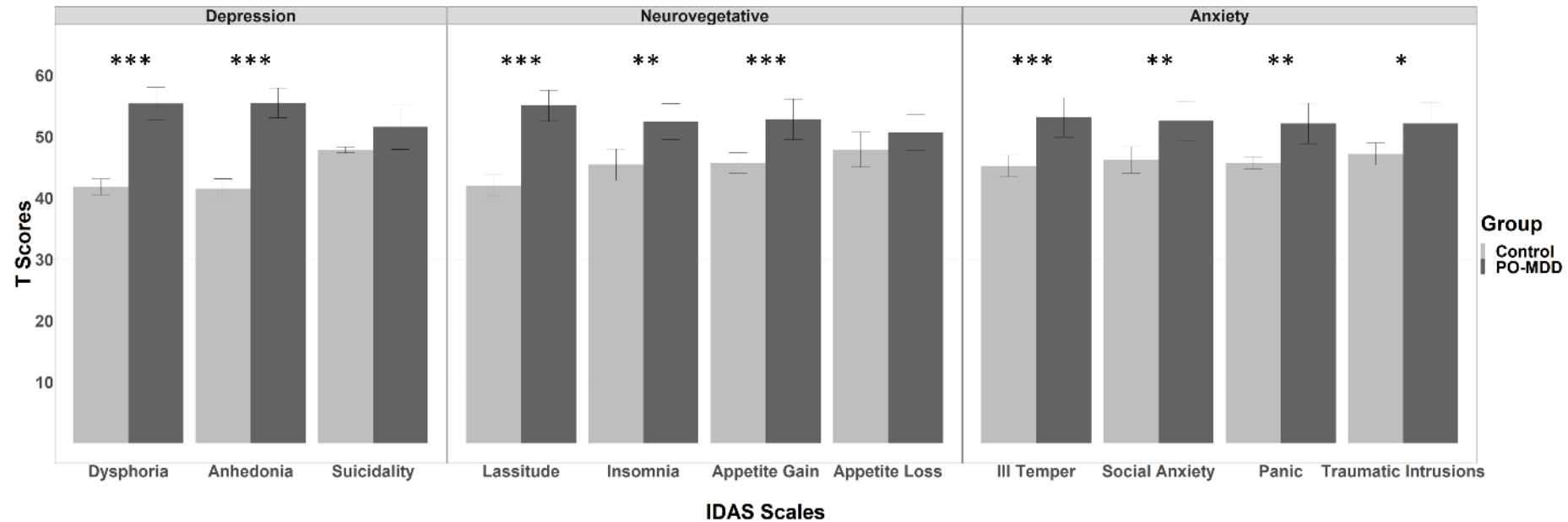
Fatigue

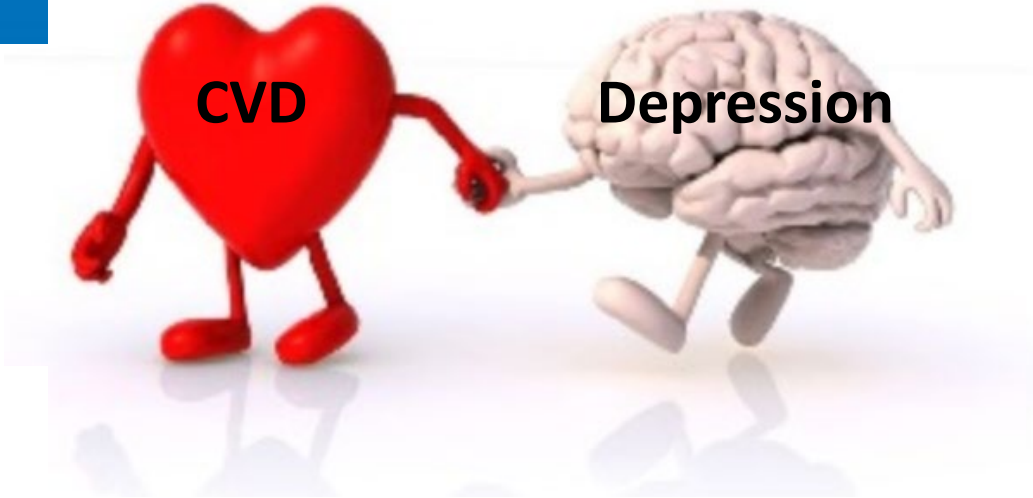
Insomnia

Appetite change

Anxiety

Panic attacks



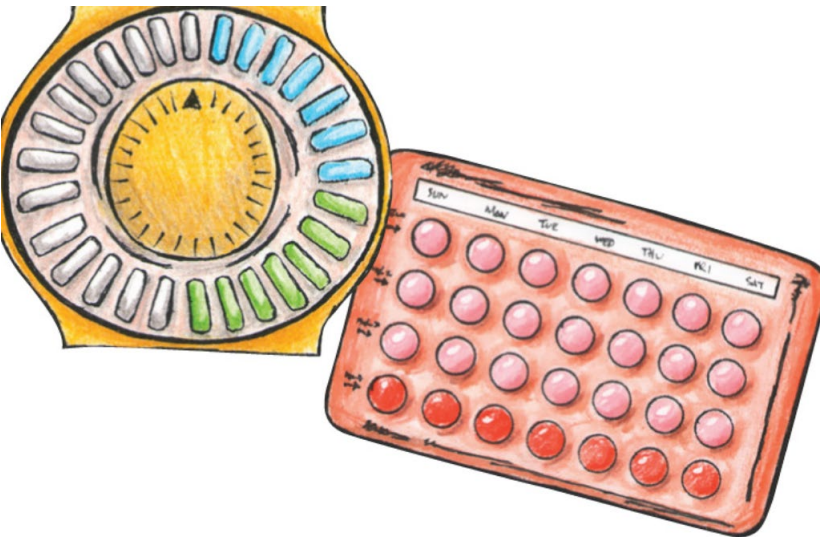


Treatment Options

Psychiatric Medications



Hormonal Treatments



Supplements/Behavioral Modification



Antidepressants and hormone therapy are the primary medication options

SSRI/SNRI best studied

Consider prior efficacy and tolerability

Hormone therapy can be very effective for mood symptoms

OCPs not well studied



Choosing an antidepressant when a patient is on tamoxifen

**Avoid
antidepressants that
inhibit CYP2D6**

**Can be helpful to
concurrently manage
mood/VMS**



VMS are common and burdensome for many women

~60% women experience VMS during the perimenopause

30% women experience severe VMS

Major impact on quality of life and function

Associated with perceived stress and alteration in stress response



Serotonergic antidepressants are helpful for vasomotor symptoms (VMS)

Venlafaxine, paroxetine, fluoxetine, escitalopram, citalopram studied

Any serotonergic agent (SSRI/SNRI) can work

Low dose is sufficient



Other non-hormonal options for VMS

Gabapentin

Clonidine

Black Cohosh

Fezolinetant



Environmental modifications can help

Identify triggers

Reduce caffeine

Reduce alcohol

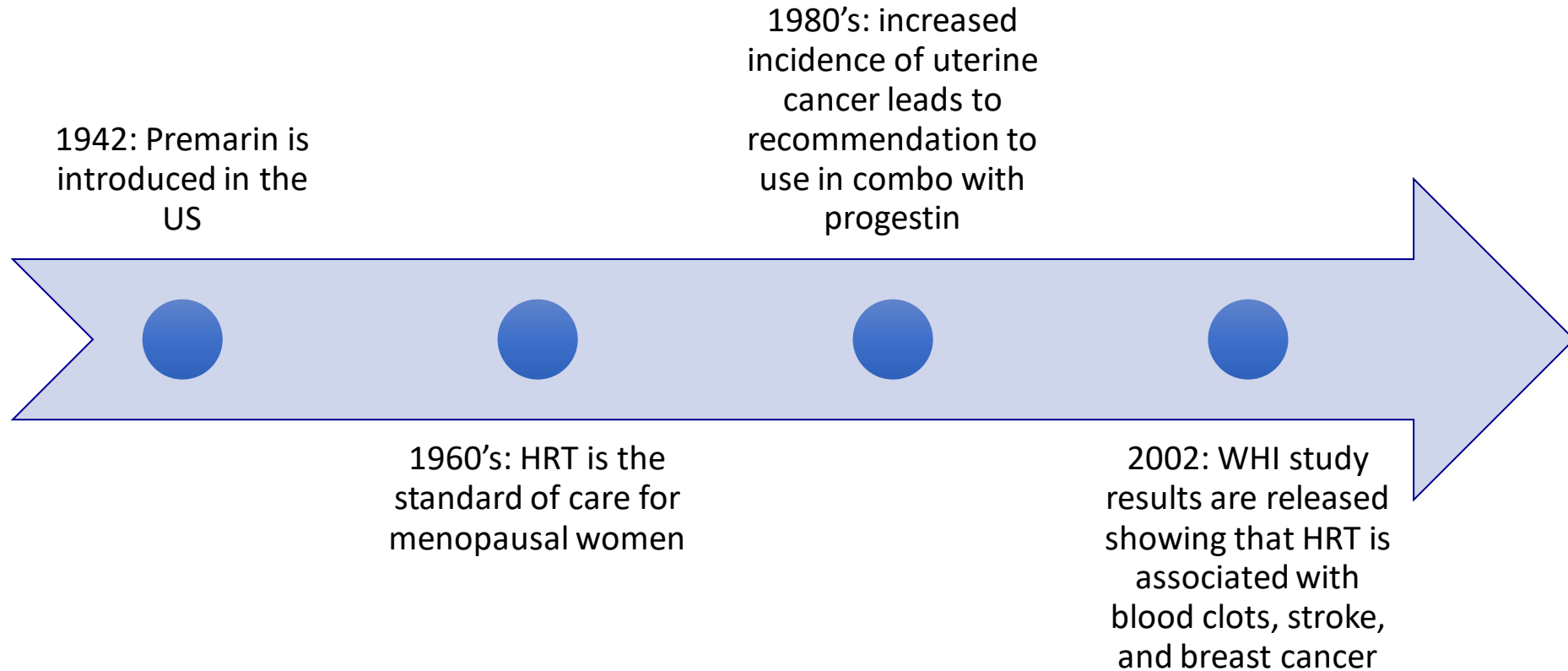
Exercise

Dress in layers

Avoid weight gain

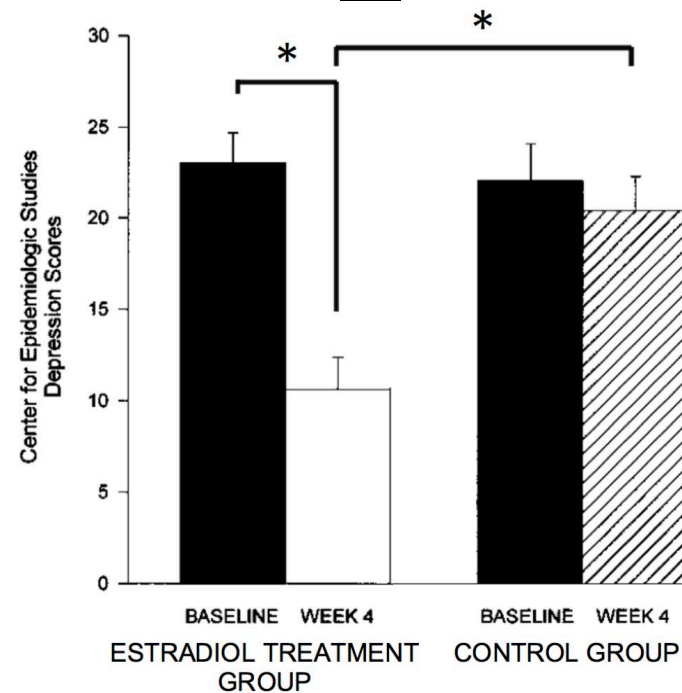


History of Hormone Replacement Therapy (HRT)



Estradiol treatment reverses depression in the perimenopause

c. Reduced depressive symptoms following estradiol treatment in women in STRAW Stage -1



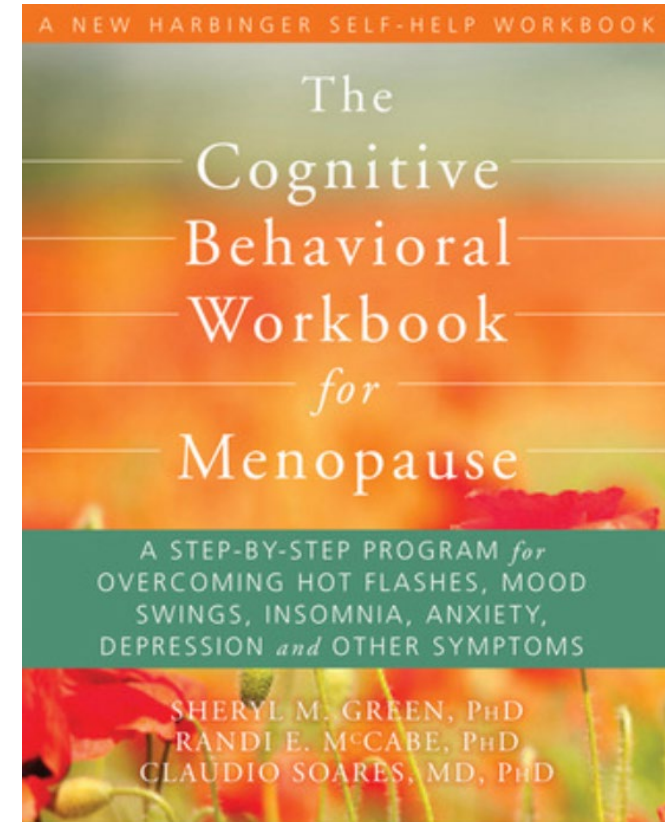
Behavioral options are effective

**Cognitive Behavioral Therapy
(CBT) has been studied for:**

Depression

VMS

Insomnia



Behavioral Activation Therapy

Behavioral activation therapy increases motivation and reduces depression at least as well as medication, even for severe depression

Behavioral activation works by helping people engage in their lives



Seek
pleasure



Make
connections



Celebrate
accomplishments

Insomnia commonly coincides with depression

30-60% women experience sleep disturbance

Can occur in the absence of VMS

Middle insomnia is most Common

Major source of functional impairment

Rate of primary sleep disorders increase in midlife



Anxiety is common and more research is needed

Limited data

Anxiety during the menopausal transition linked with more significant vasomotor symptoms

Linked to increased risk for cardiovascular disease



Bipolar Disorder

Women with bipolar disorder are at an increased risk for affective exacerbation

Some studies have identified the late perimenopause and early postmenopause as the periods of highest risk

Depressive episodes are the most common

Exacerbations not been correlated with specific hormone profiles



Conclusions

Some women are vulnerable to mood symptoms during reproductive transitions

PMDD is diagnosed clinically and there are both hormonal and non-hormonal options

Depressive symptoms during perimenopause are common

Antidepressants can be used to address both depressive and menopausal symptoms

Questions?