The Menstrual Cycle and Mental Health: *Health Service Priorities*

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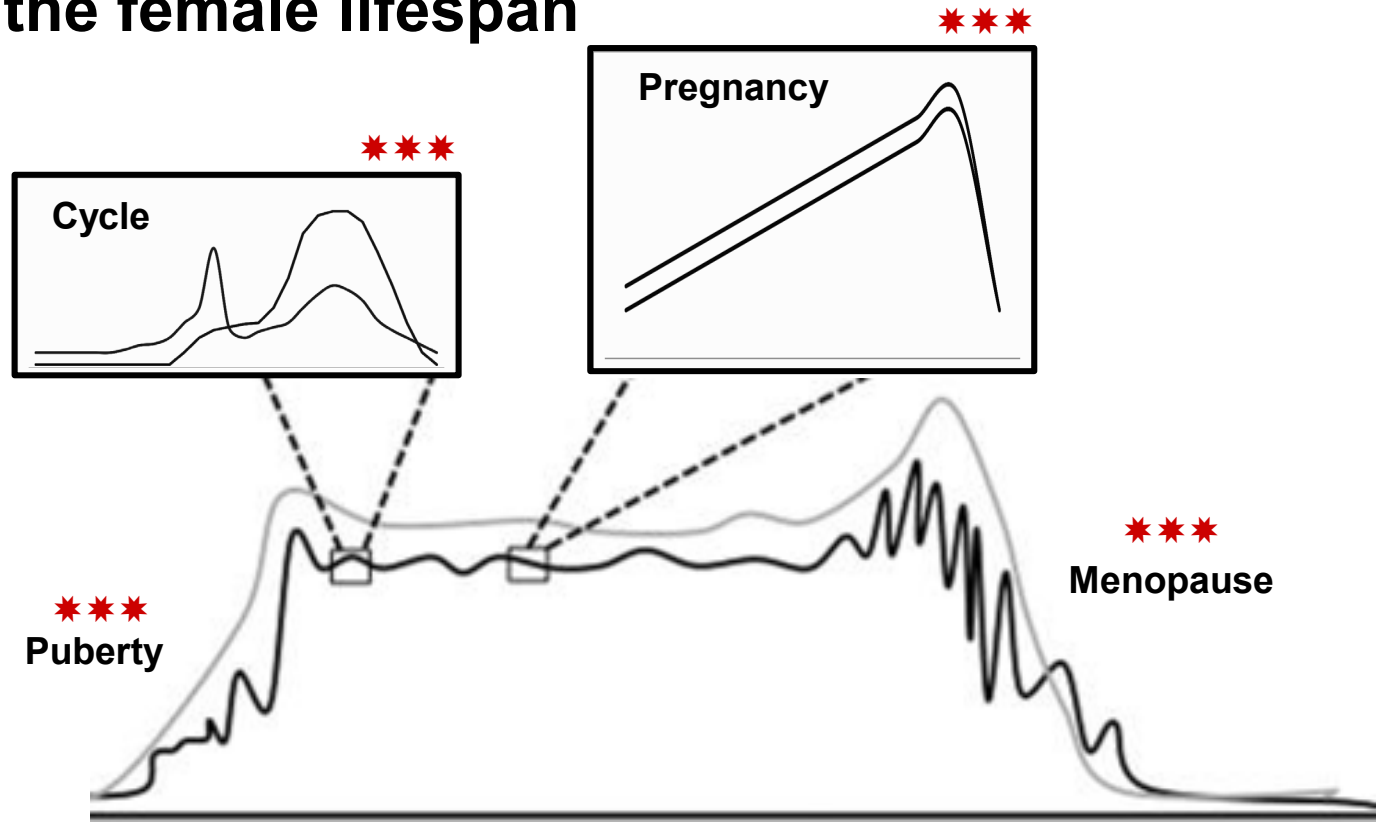
Funding and Disclosures

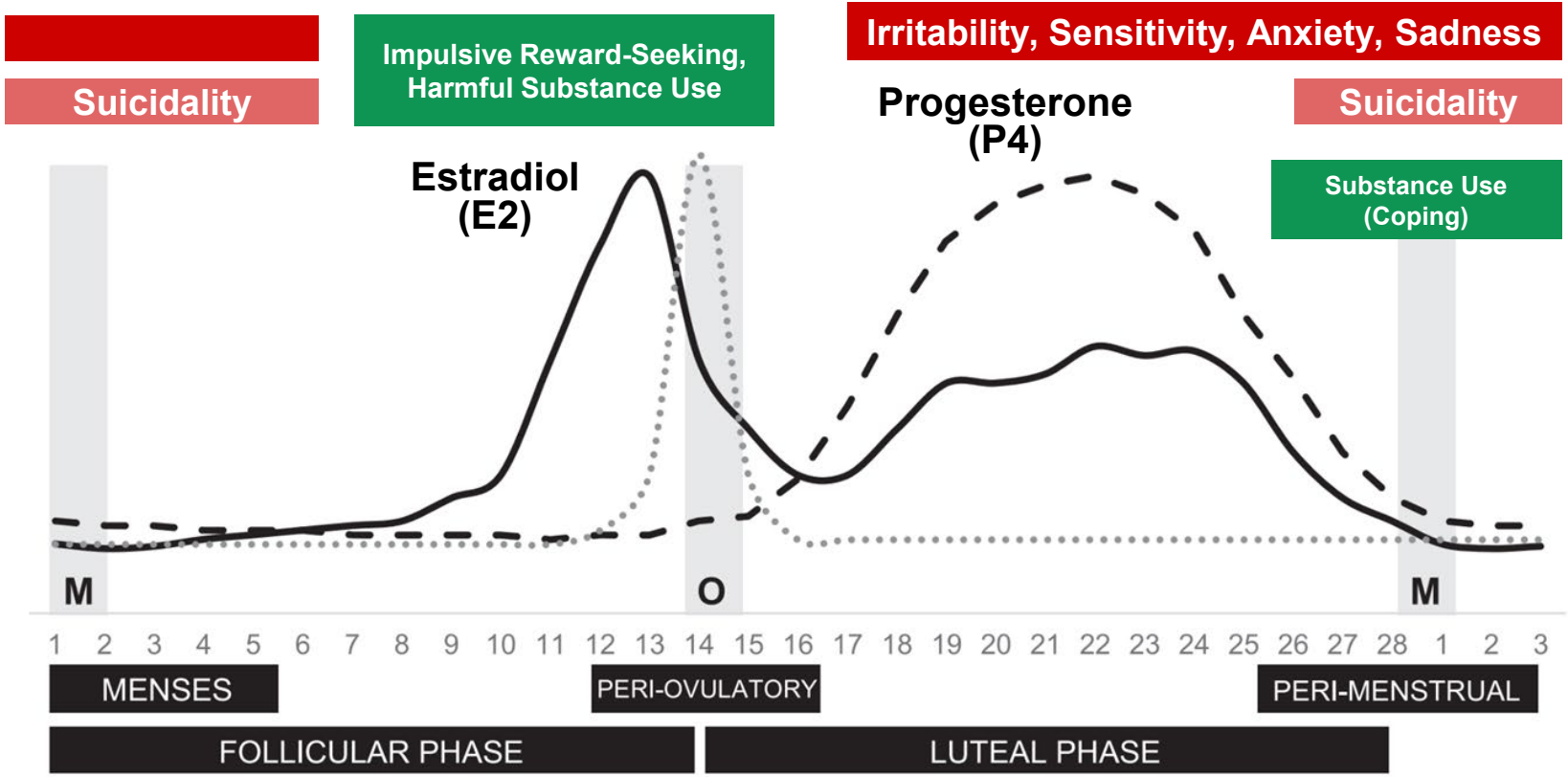
- I have no financial conflicts of interest to disclose
- I have served as the volunteer clinical advisory board chair at IAPMD since 2016
- This work was funded by a number of NIH grants:
  - K99/R00MH109667, R01MH120843, R01MH122446, R01MH126940, R01MH119119, R01AA027990, R01MH128238
- My laboratory's logo indicates findings from my group.
  - www.clearlabresearch.com

Ovarian steroid fluctuations correlate with emotional risk across the female lifespan



PMIDs: 27347888

The menstrual cycle triggers significant emotional and behavioral changes in *some people, but not all*



Premenstrual Dysphoric Disorder (PMDD) is the sole diagnostic entity

Added to DSM-5 in 2013… added to ICD-11 in 2022

At least 5 (at least one emotional) of the symptoms below must be present in the week before menses AND minimal or absent in the week post-menses:

1. Marked affective lability
2. Marked irritability, anger, or conflicts
3. Marked depressed mood *(least common)*
4. Marked anxiety

1. Decreased interest in usual activities
2. Difficulty concentrating
3. Lethargy, fatigability, lack of energy
4. Marked change in appetite
5. Hypersomnia or Insomnia
6. Feeling overwhelmed or out of control
7. Physical symptoms (swelling, pain, bloating)

➔ Distress OR impairment

➔ Pattern confirmed across 2 cycles of daily ratings

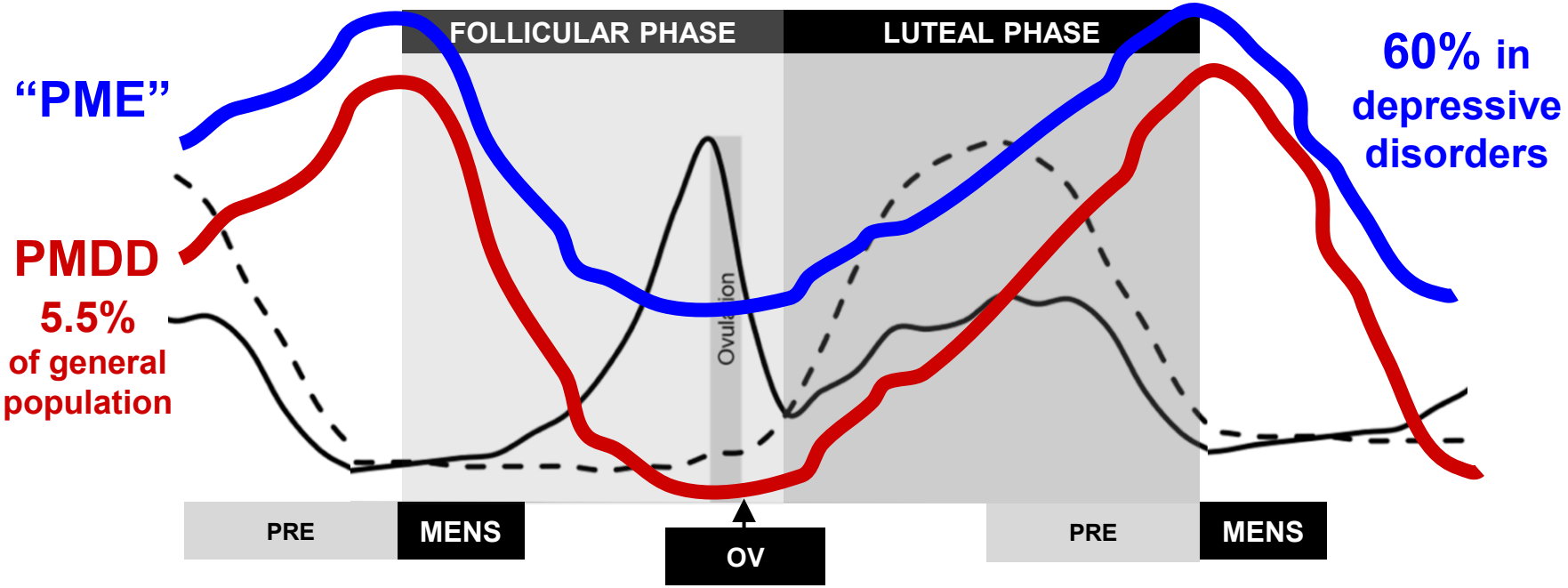
➔ NOT only an exacerbation (although it may co-occur)

➔ NOT during hormone use

PMID: 22764360

PMDD is prevalent, and PME is even more prevalent

PME accounts for the majority of clinical referrals, transdiagnostic



PMIDs: 15385694, 18366818, 35936817, 35867164

Functional Impact of Premenstrual Disorders (PMDs)

~7 ½ yrs of symptoms across a typical reproductive life

Most common/impairing symptoms: irritability, interpersonal sensitivity, stress reactivity, poor concentration, fatigue

Relationship Damage most common (partner, child, friends)

"I worry about effects on my ten-year-old—my husband can leave, but my daughter can't." - Patient

Occupational Damage (school, work, career)

"I left so many jobs because I got so angry, I needed to quit or fell out with colleagues or upset customers." - Patient

PMIDs: 12892987, 28193300; 10565662; Quotes adapted from https://us.macmillan.com/books/9781250882899/thecycle

PMDs are associated with suicide risk

In 599 pts recruited for PMDD:

87% reported lifetime suicidal ideation

34% **reported** lifetime suicide attempt

In 128 pts recruited for suicidal ideation:

62% demonstrated PME *(>=30% change)*

History of attempt (vs. ideation only) predicts greater premenstrual worsening

Review of hospital studies indicates that risk of **hospitalization for suicide attempt** peaks during menses

PMIDs: 35303811, 38093647, 16573848

STANDARD OF CARE

Daily tracking is <u>required</u> for PMDD diagnosis, but this is not feasible in most clinical settings

~60% false positives

Structured Interviews

PREMENSTRUAL DYSPHORIC DISORDER (PAST 12 MONTHS)	PREMENSTRUAL DYSPHORIC DISORDER CRITERIA		
IF SUBJECT IS A BIOLOGICAL MALE, POST-MENOPAUSAL FEMALE, PREGNANT FEMALE, OR FEMALE WITH HYSTERECTOMY PLUS OOPHORECTOMY, CHECK HERE ___ AND SKIP TO NEXT MODULE.			A172
Looking back over your menstrual cycles for the past 12 months, since (1 YEAR AGO), **have you had mood symptoms such as anger, irritability, anxiety, or depression that developed before your period and then went away during the week after your period?** *IF YES*: **After your period began, did the problems disappear for at least a week?**	A. In the majority of menstrual cycles, at least five symptoms must be present in the final week before the onset of menses, start to improve within a few days after the onset of menses, and become minimal or absent in the week postmenses. NOTE: If number of days of symptoms is 20 per month or greater, recheck symptom-free and symptom present intervals.	? 1 2 3 GO TO NEXT MODULE	A173

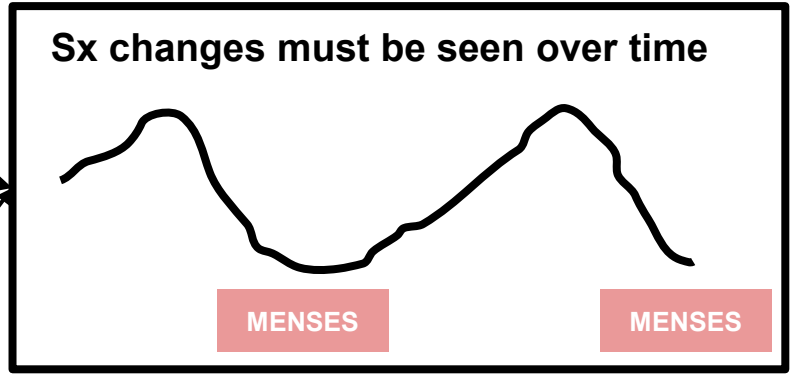
Single Time Point Survey

The premenstrual symptoms screening tool (PSST)

(please mark an "X" in the appropriate box)

Do you experience some or any of the following premenstrual symptoms which *start before* your period and *stop* within a few days of bleeding?

Symptom	Not at all	Mild	Moderate	Severe
1. Anger/irritability				
2. Anxiety/tension				



… just 12% of surveyed clinicians said they used daily ratings for diagnosing PMDD.

PMIDs: 27523500, 24512469, 33978482, 33651443

STANDARD OF CARE

Evidence-Based Treatments

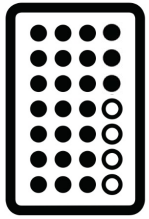
Hormones are normal; treatments buffer neural sensitivities or eliminate cycling hormones

SSRIs in luteal phase only or full cycle

- Rapid serotonergic onset of action, FDA-approved; ~60% benefit

Drospirenone + Ethinyl Estradiol Oral Contraceptive ("Yaz"; 24-4 dosing)

- Suppress ovulation, 24-4 dosing; FDA-approved; smaller benefit



Symptom-Focused Therapies (e.g., quetiapine, CBT/DBT)

GnRH Agonist + Stable E2/P4 addback (Chemical Menopause)

- FDA approval not sought despite meta-analytic support for efficacy
- Symptoms recur in 1st month addback, then remit
- Sometimes made permanent through **TH/BSO + E2 addback**

PMIDs: 23744611, 12411222, 37341478, 37365881, 28427285, 15198787;

ACOG Guidelines: https://www.acog.org/clinical/clinical-guidance/clinical-practice-guideline/articles/2023/12/management-of-premenstrual-disorders

IMPROVING ACCESS

Addressing General Barriers & Diagnosis

Implement mandatory PMD healthcare training

- Introduced in 2013, not standard training in Ob Gyn or Psychiatry
- *Targets*: Primary Care, Psychiatry, OB/GYN, Clinical Psychology, Social Workers/LCSWs, Pediatrics

Develop automated, sustainable diagnostic tools

- Need for centralized, sustainable funding for diagnostic apps

Refine diagnosis to address more common PME

Set lifespan screening milestones

Boost workforce through nonprofit partnerships

- Currently, reproductive mental health expert volunteers (www.ncrp.org) and nonprofits (e.g., www.iapmd.org) do the majority of trainings

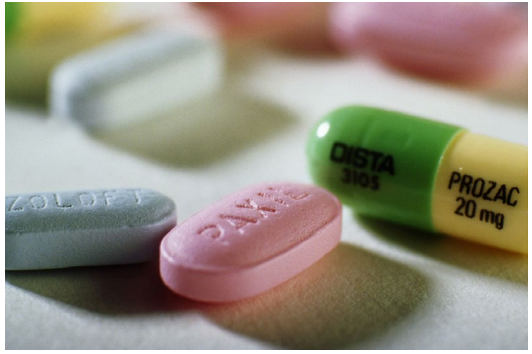
PMIDs: 24512469, 35354450, 27523500, 33978482; https://osf.io/preprints/osf/hp7mn

IMPROVING ACCESS

Addressing Barriers to SSRI treatment in PMDD

Train providers in use of SSRIs

- Most providers start with OCs despite evidence SSRIs more effective
- Favorable risk/benefit ratio in pregnancy
- Some also reduce menopausal hot flashes



Educate patients in mechanisms of action

- Patients fear SSRI represents “band-aid”/misdiagnosis
- Experiments demonstrate serotonin mechanism

Facilitate navigation of SSRI side effects

- *Educate*: many temporary, related to specific SSRI
- *Switch?:* Long-term concerns most often include sexual dysfunction and weight or sleep changes

PMIDs: 3744611, 28649145, 12411222, 15014625

IMPROVING ACCESS

Addressing Barriers to Hormonal Contraception in PMDs

Refine Tx guidelines to be more specific regarding COCs

- Specify formulation (drospirenone + EE), schedule (24-4)
- See recent expert review from Rapkin et al.

Train providers in benefits and risks of hormones

- Despite benefits in RCTs, negative mood reactions common
- Monitor for adverse mood changes
- Patients with depression history at greater risk

Test <u>new</u> hormonal contraceptive options for PMDD

- Many patients cannot safely take estrogens
- Newer progestin-only pills that suppress ovulation (drospirenone, desogestrel) could be tested, would be more accessible

COC = Combined Oral Contraceptive; PMIDs: 31572029, 28816924; 27680324; 29145752

IMPROVING ACCESS

Addressing Barriers to Chemical Menopause Tx

Provide PMD-specific GnRHa Training

- Train reproductive psychiatrists and gynecologists in GnRHa for PMDD
- See recent instructional guide →

Incentivize greater collaboration among Ob/Gyn & Psychiatry in repro mental health

Disseminate existing chemical/surgical menopause resources to tx-resistant patients

- Reduce fear, increase willingness
- e.g., www.iapmd.org/surgery

Test <u>new</u> GnRH *antagonists* for PMDD

- Oral elagolix untested but may increase access, eliminate agonist side effects

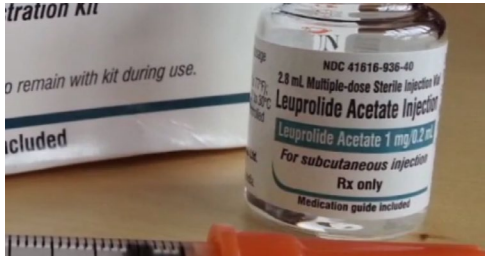
Review > J Clin Psychiatry. 2023 Jun 21;84(4):22r14614. doi: 10.4088/JCP.22r14614.

What's Stopping Us? Using GnRH Analogs With Stable Hormone Addback in Treatment-Resistant Premenstrual Dysphoric Disorder: Practical Guidelines and Risk-Benefit Analysis for Long-term Therapy

Melissa Wagner-Schuman [1 2 3], Alyssa Kania [1], Jordan C Barone [1], Jaclyn M Ross [1], Ashley Mulvihill [1], Tory A Eisenlohr-Moul [1]

Affiliations + expand

PMID: 37341478 DOI: 10.4088/JCP.22r14614



PMIDs: 37341478

Thank You!