



— YOUTUBE RESEARCH SUMMARY

Research Summary: Perimenopause Symptoms

As featured in Dr. Kenny Mittelstadt's video: [Why Your Perimenopause Symptoms Keep Getting Misread](#)

— Research Context

Perimenopause symptoms are one hormonal terrain pattern producing five different readings across five different offices, and the research increasingly supports that framing. The core issue during the transition is that the hormonal signal becomes erratic, swinging up and down in ways the body's tissues are calibrated to detect at an extraordinarily precise level. The key studies below help connect these dots and explain why so many women in this phase end up with partial answers, multiple prescriptions, and no one connecting the whole picture.

— Key Findings from the Research

STUDY 1 • PMID 31693131

Joffe and colleagues tracked perimenopausal women over time, measuring estrogen and progesterone levels weekly alongside mood symptoms. Estrogen variability, the swings up and down rather than a steady decline, most strongly predicted depression severity. A woman whose estrogen levels were jumping around week to week was significantly more likely to experience depression than one whose levels were simply lower but stable. When progesterone also declined, the effect compounded further. Anxiety, low mood, and emotional dysregulation during perimenopause are frequently referred to mental health specialists as standalone concerns. This research frames them instead as a hormonal signal instability problem: the brain is responding to an unstable input rather than generating a primary mood disorder.

STUDY 2 • PMID 33095879

Santoro and colleagues reviewed the menopausal transition and examined how wide fluctuations in reproductive hormones, beyond eventual decline, produce the full symptom cluster most associated with this phase. The same hormonal turbulence driving hot flashes and night sweats also drives mood disruption, temporary cognitive changes, and genitourinary changes, which can appear in any combination, in any order, often simultaneously. That variability in presentation is exactly why the specialist model struggles: symptoms show up in different offices because they affect different body systems, yet they originate from the same upstream source. Vasomotor symptoms affect roughly 80% of women during the transition, with around 4 in 10 describing them as severe enough to significantly disrupt daily life.

STUDY 3 • PMID 37553173

Duralde and colleagues, writing in the BMJ in 2023, noted that the link to menopause may even be elusive, meaning clinicians themselves frequently fail to connect a patient's symptoms to the menopausal transition. Symptoms remain substantially undertreated across the board, and the diagnostic gap spans all specialties. It is built into how the transition has been conceptualized and taught across medicine. This reframes the conversation: the problem is a fragmented framework, one that has yet to standardize how to read the transition as a whole-system event. Fragmented care is the predictable result of that fragmented framework, not a failure of individual clinical attention.



— Functional Medicine Connections

Estrogen functions as a regulatory touchpoint across the brain, the cardiovascular system, connective tissue, and metabolism. The cells and tissues that respond to it are calibrated to detect it at concentrations measured in trillionths of a gram per milliliter of blood. When the signal becomes unreliable, every system that depended on that stabilizing influence begins to show the strain.

This is why the symptom picture during perimenopause so often looks multisystem. Weight that stops responding to previously effective strategies, joint discomfort that feels different from before, brain fog that sleep does not fully resolve, early bone density changes, palpitations with no cardiac finding: these are clinical signals that each appear to be a separate problem when read one at a time. Read together, through the lens of what estrogen provides as a buffering and anti-inflammatory hormone, they form a recognizable pattern.

The stress chemistry layer compounds this further. The body's stress-response system, managed through a network sometimes called the HPA axis, shares regulatory territory with the reproductive hormone system. A woman who has been running at high output for years, with chronically elevated stress hormones in the background, arrives at this transition with less hormonal reserve to buffer the volatility. The stage for how difficult the transition feels can be set years before the symptoms become unmistakable. Testing adds another layer: FSH, the marker most commonly used to evaluate where someone is in the transition, is a single-point snapshot of a moving target. FSH values can shift significantly from day to day within a single cycle during perimenopause, and a result within the normal reference range on the day of the draw may be flanked by elevated readings the day before and the day after. Tools that track hormone levels and their breakdown products across a full cycle reveal the pattern that a single result cannot.

— Practical Reflections & Takeaways

If you have been managing what feels like separate symptoms in separate offices, with each workup returning results that are normal or inconclusive, it may be worth asking whether anyone has looked at these readings together, across a full cycle, with the whole picture in front of them.

When you think about your own symptom timeline, does the sequence make more sense when you read it as one shifting pattern rather than several unrelated problems arriving at the same time? Your lived experience of that pattern is meaningful data, and it deserves a framework that can hold all of it at once.

— References

- Joffe, H., de Wit, A., Coborn, J., et al. Impact of estradiol variability and progesterone on mood in perimenopausal women with depressive symptoms. *The Journal of Clinical Endocrinology and Metabolism*. 2020;105(3):e642-e650. PMID: 31693131.
- Santoro, N., Roeca, C., Peters, B. A., et al. The menopause transition: Signs, symptoms, and management options. *The Journal of Clinical Endocrinology and Metabolism*. 2021;106(1):1-15. PMID: 33095879.
- Duralde, E. R., Sobel, T. H., Manson, J. E., et al. Management of perimenopausal and menopausal symptoms. *BMJ*. 2023;382:e071896. PMID: 37553173.

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