The Gut-Hormone Connection

A Clinician's Guide to Menopausal GI Health

Beyond HRT — A Stepwise Approach to Gut Health in Menopause

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Who's Behind the Conversation

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- IFM Certified Physician & Educator
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- Founder, Dr Vivian Asamoah Integrative Functional Gastro

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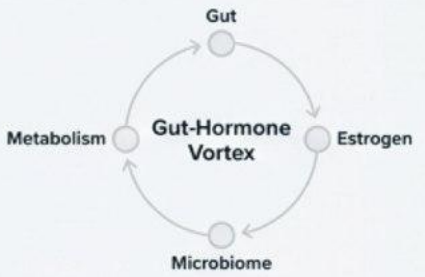
- Board-certified Obstetrician-Gynecologist (FACOG)
- Menopause Society Certified Practitioner (MSCP)
- MBA · Certified Physician Executive (CPE) · Professional Certified Coach (PCC)
- Focus: midlife hormonal & metabolic health; integrates GYN care with interdisciplinary referral

The Clinical Gap: Treating Systems, Failing the Patient

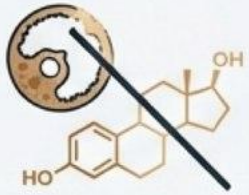


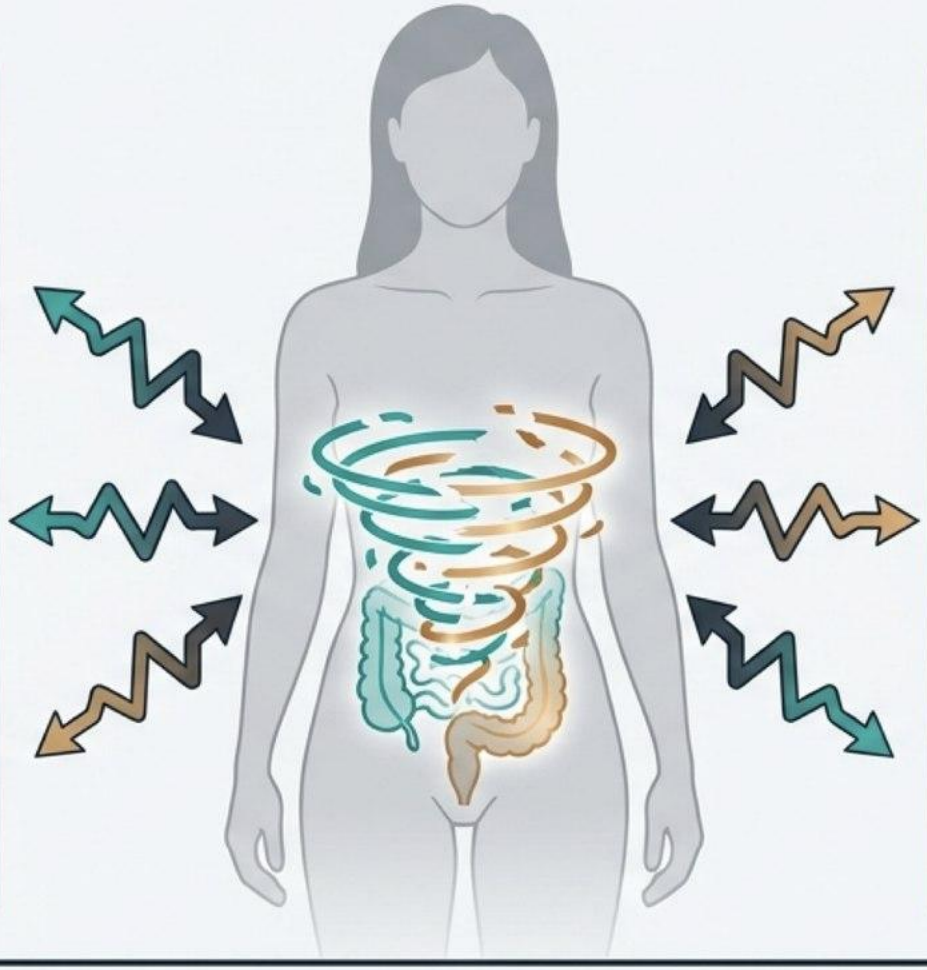
Gastroenterology

Sees:
- Bloating, altered motility, newly diagnosed IBS.

Treats:
- The symptom (antispasmodics, laxatives, low-FODMAP).

Misses:
- The **hormonal root cause.**

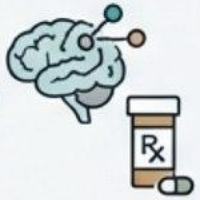




Gynecology

Sees:
- Vasomotor symptoms, mood shifts, vaginal atrophy.

Treats:
- The symptom (HRT, SSRIs).



Misses:
- The **impaired gut metabolism** causing **systemic inflammation.**

Midlife GI distress cannot be resolved while the gut and the ovaries are treated as isolated systems.

Disclosures

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Why the Gut-Hormone Axis Isn't in Standard Training

Perimenopause and menopause bring fatigue, brain fog, bloating, altered motility, food sensitivities, weight gain, and shifting insulin sensitivity, changes that are typically managed in silos because the gut-hormone-metabolism link isn’t part of standard training.

60–86%

of women who seek help for these symptoms feel dismissed by their clinician

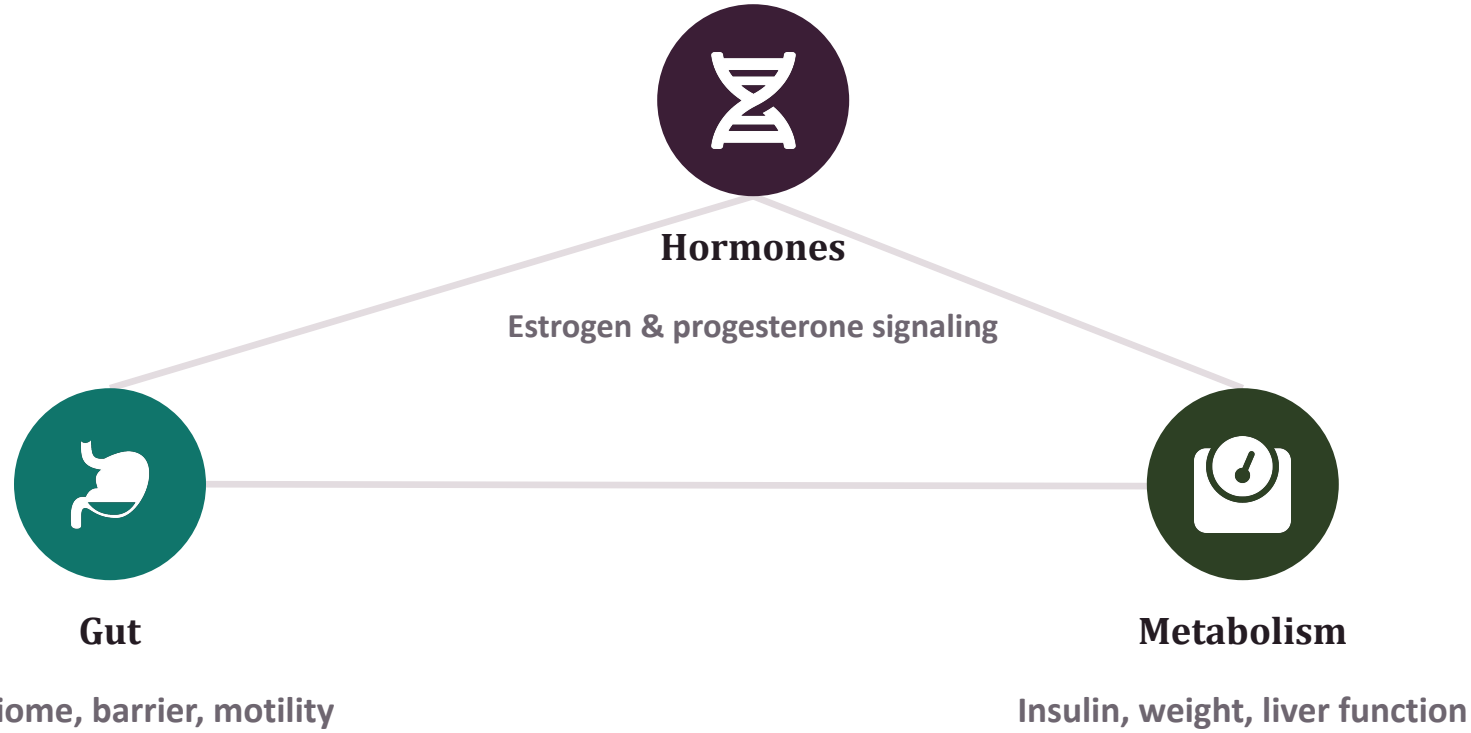
6.8%

of physicians feel adequately trained to manage the menopause transition

Objectives:

1	**Differentiate**	Describe how perimenopausal/menopausal hormonal change affects gut motility, the microbiome, and hepatic/metabolic function — to differentiate menopause-related GI symptoms from other GI pathology.
2	**Sequence**	Apply a stepwise, evidence-based counseling framework that sequences hormone therapy, nutrition, and lifestyle change to improve adherence and avoid overwhelm.
3	**Screen & Refer**	Select appropriate baseline labs and identify red flags warranting specialist referral, including age-appropriate colorectal cancer screening.
4	**Coordinate Care**	Formulate an interdisciplinary care and referral plan for patients on HRT and/or GLP-1 receptor agonists, with communication strategies across GYN, primary care, and GI.

The Gut-Hormone-Metabolic Axis



A change in one node moves all three. The gut alone houses ~70% of the immune system and produces most of the body's serotonin and dopamine, so a single-system workup routinely misses the diagnosis in midlife women.

Perimenopause vs. Menopause: Two Different Physiologic States

PERIMENOPAUSE

Chaotic Hormonal Swings

- Lasts 7–10 years before the final period
- Erratic estrogen, unpredictable spikes and crashes, not a steady decline
- Hypothalamus detects declining ovarian reserve
- Anxiety, brain fog, GI changes, and mood shifts

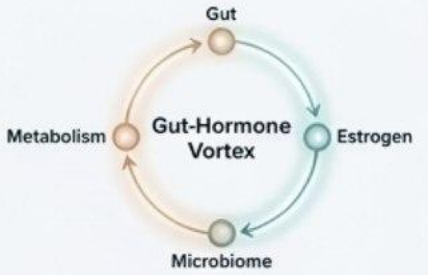
MENOPAUSE

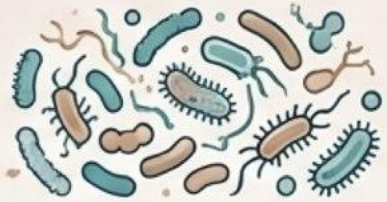
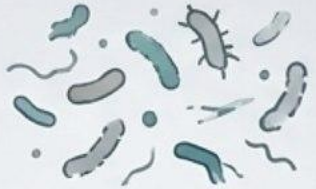
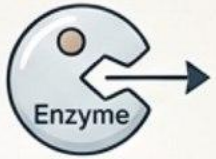
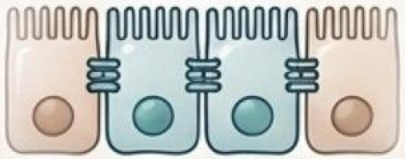
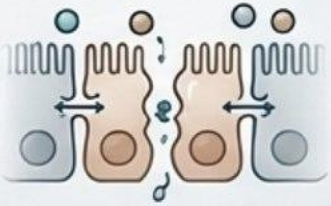
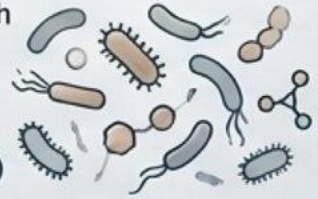
Consistently Low Estrogen

- Defined by 12 consecutive months without a period
- Rising FSH & LH as the pituitary works harder
- Cognitive changes: brain fog, memory lapses
- Systemic risk: metabolic shifts, bone loss, CVD, genitourinary changes

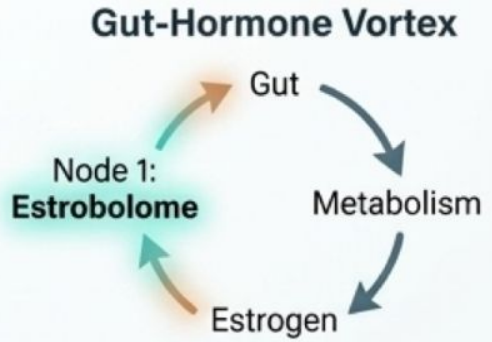
Clinical pearl: diagnose perimenopause by menstrual history, NOT LABS. FSH fluctuates too much in this window to be reliable.

The Biological Shift: Pre- vs. Post-Menopausal Milieu

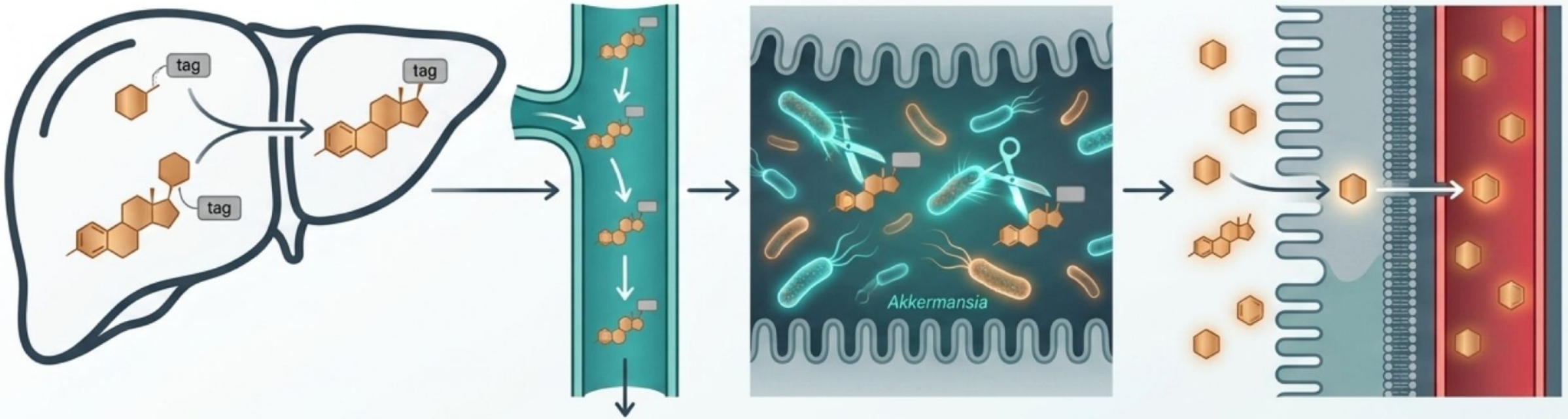


	Pre-Menopause	Post-Menopause
Microbiome Diversity	**High** richness and stability 	 **Low** diversity, male-like profile
Estrobolome Activity	**Regulated GUS** enzyme activity 	 **Dysregulated**, loss of *Akkermansia muciniphila*
Barrier Integrity	**Intact** tight junctions 	 **Compromised**; elevated FABP2 & sCD14
Vaginal pH	 **Acidic**, *Lactobacillus*-rich 	  **Alkaline**, diverse/anaerobic, decreased lactic acid

Mechanism 1: The Estrobolome & Enterohepatic Recycling



The Enterohepatic Recycling Plant



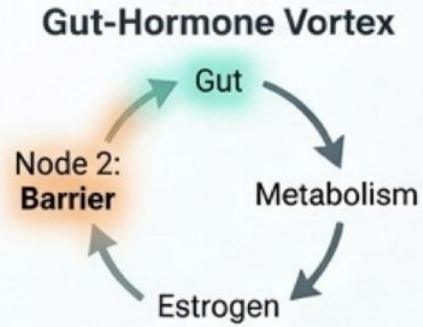
Phase 2 Liver Conjugation: Estrogen is tagged with glucuronide to make it water-soluble for excretion.

Biliary Tract

The Molecular Scissors: Gut bacteria produce beta-glucuronidase (GUS).

Reactivation: GUS deconjugates estrogen, allowing active hormone to be reabsorbed. Crucial for maintaining systemic estrogen levels.

Mechanism 2: Gut Barrier Failure & Permeability

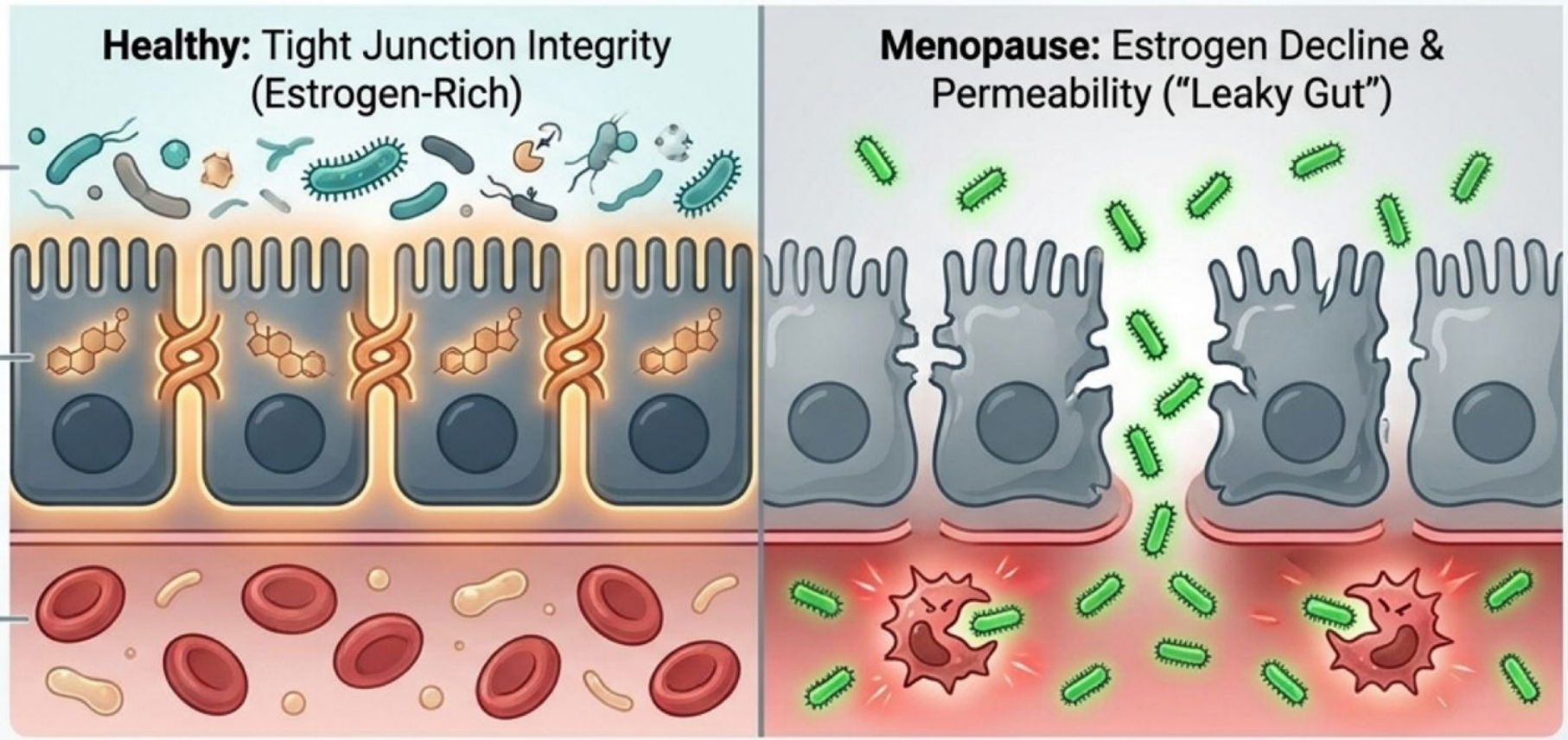


The Barrier Breach

Estrogen is structural.
It maintains the integrity of epithelial tight junctions.

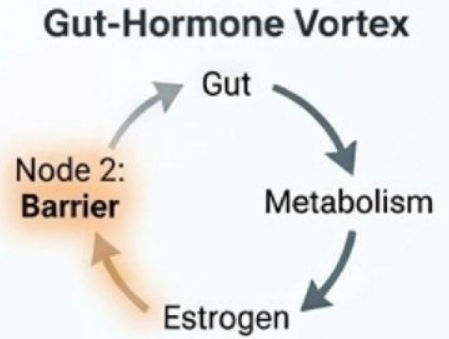
As estrogen declines,
the gut barrier becomes permeable ('leaky').

Lipopolysaccharides
(LPS) from Gram-negative bacteria translocate into the bloodstream, triggering systemic immune activation (TLR4 pathway).

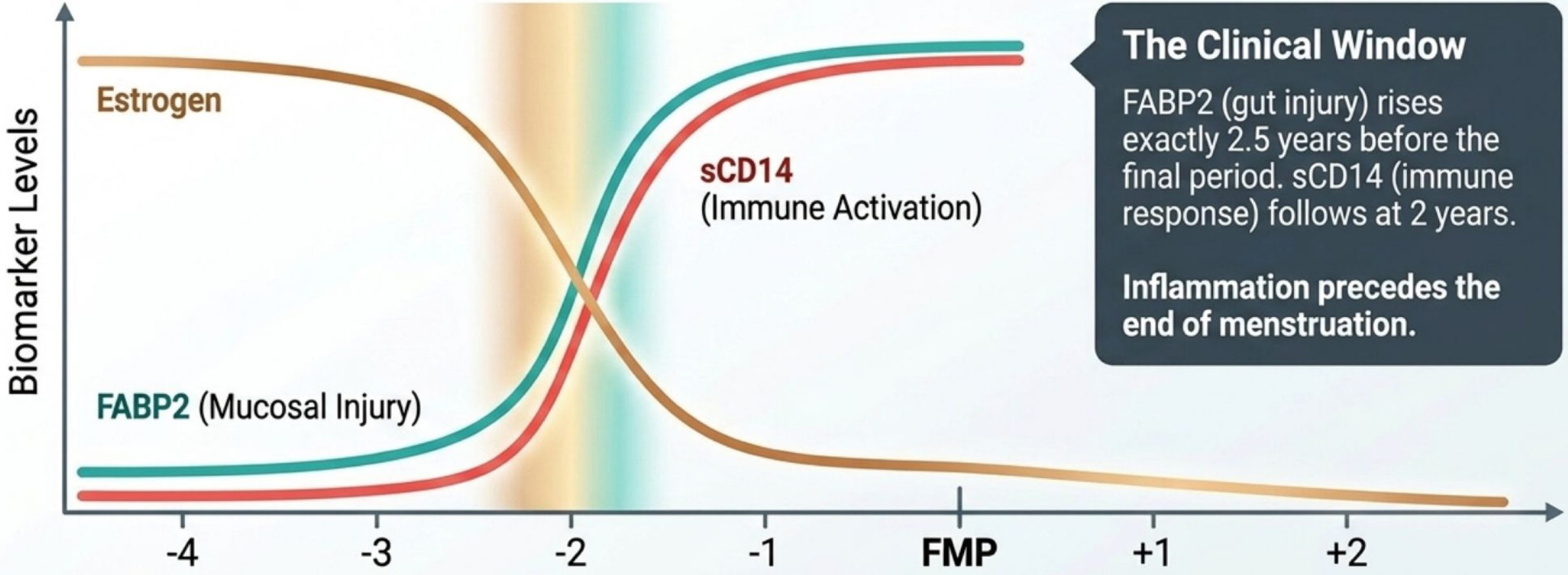


The 2026 SWAN Cohort: The "Leaky Gut" Trajectory

964 women tracked through the menopausal transition (JCI, 2026).



The Activation Timeline



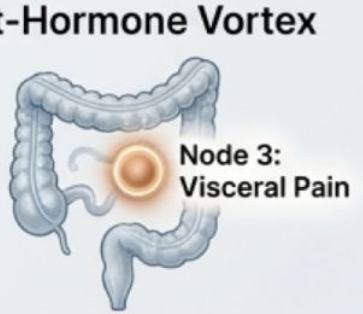
The Clinical Window

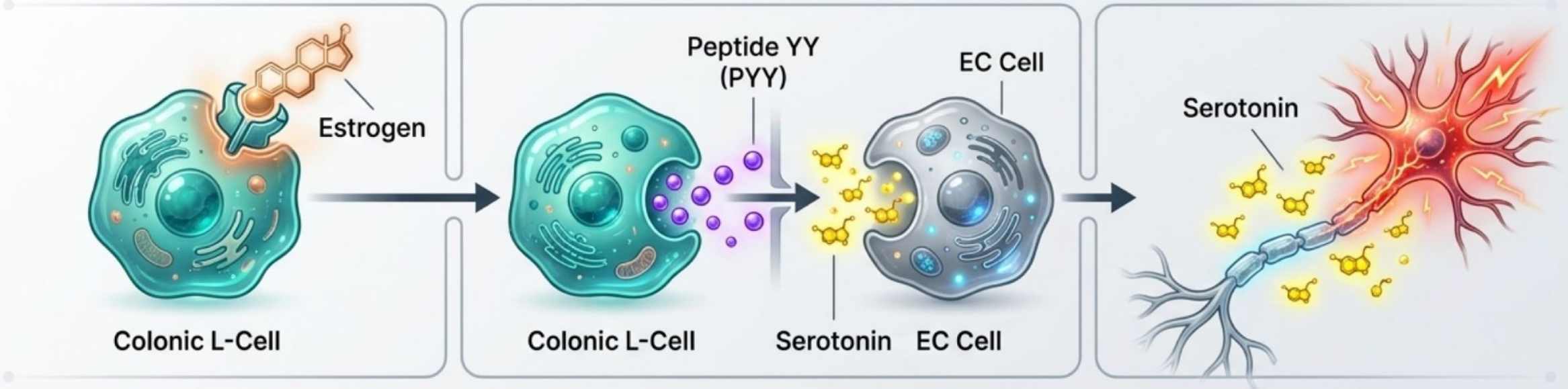
FABP2 (gut injury) rises exactly 2.5 years before the final period. sCD14 (immune response) follows at 2 years.

Inflammation precedes the end of menstruation.

Mechanism 3: Visceral Pain & Hormonal Signaling

The UCSF Science Study on Gender-Specific IBS (Ingraham & Julius, 2024).





Step 1: Estrogen directly binds to receptors on colonic L-cells.

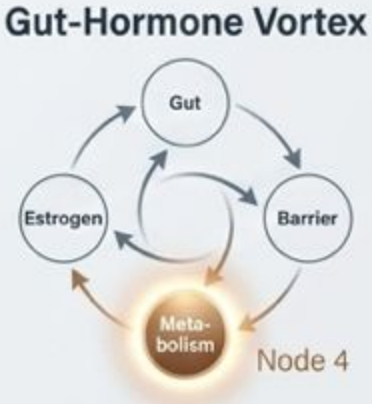
Step 2: L-cells release Peptide YY (PYY), triggering EC cells to release serotonin.

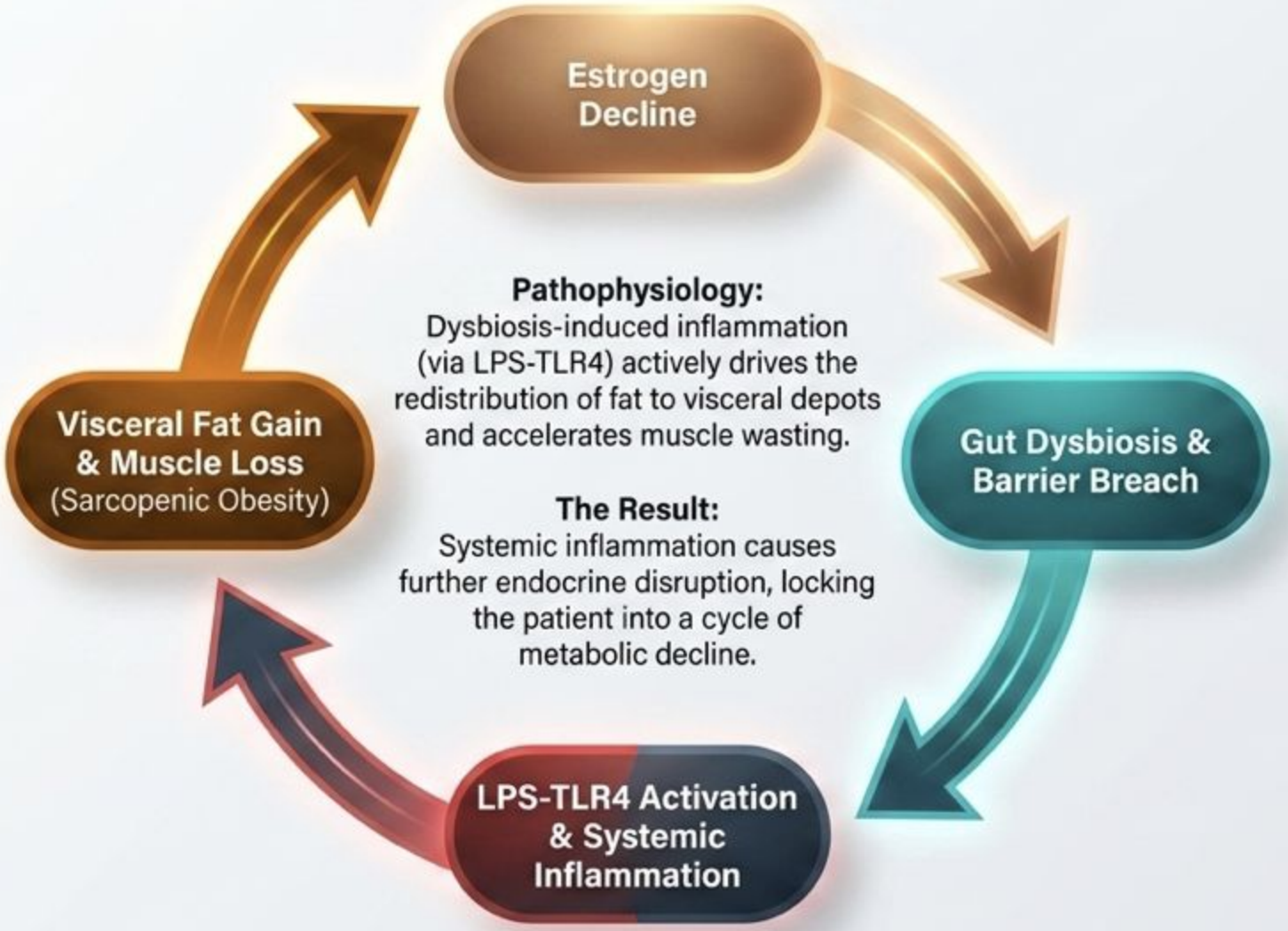
Step 3: Serotonin hyper-activates pain-sensing nerve fibers.

Takeaway: Fluctuating estrogen during perimenopause acts as as an **unpredictable 'volume dial'** for gut pain.

Mechanism 4: The Metabolic-Gut Axis

The “Microbiota-Estrogen-Adipose” Axis (*PMC Biomedicines*, 2024).





Vignette 1 - Jenny

Doc, is it time for me to start MHT?

46-year-old: irregular cycles, fatigue, bloating, and new-onset constipation.

VIGNETTE 1 · Jenny's Story

Diagnose Perimenopause Clinically

The menopausal transition is defined by a persistent >7-day change in cycle length (early transition), progressing to >60 days of amenorrhea (late transition).

Menstrual pattern : ask about her last 3 cycles

- Onset and duration of cycle-length change
- Skipped cycles?
- Heavy or intermenstrual bleeding
- Postcoital bleeding?

Vasomotor, sleep & mood clues

- Hot flashes and night sweats are most likely to rule it in, but their absence does not rule it out
- ~10% of perimenopausal women experience major depression, which independently causes constipation and fatigue

VIGNETTE 1 · Jenny's Story

Tracking Symptom Burden: The Greene Climacteric Scale

A validated tool to quantify menopause symptom burden across 21 symptoms: useful for objectifying "which symptom is most bothersome" before you sequence treatment.

Four Symptom Domains

- Psychological — anxiety, mood, cognition
- Physical — fatigue, muscle/joint symptoms
- Vasomotor — hot flashes, night sweats
- Sexual function

Scoring & Clinical Use

- Each symptom scored 0 (not at all) to 3 (extremely)
- Establish a baseline at the initial consult
- Reassess every 4–6 weeks to see whether the stepwise plan is working before adding the next intervention

VIGNETTE 1 · Jenny's Story

Baseline Workup for Fatigue/ Brain Fog /Bloating + Constipation

CORE LABS — DRIVEN BY THE TWO NON-SPECIFIC SYMPTOMS

- CBC + CMP
- iron panel/ferritin
- TSH, Free T4, T3 ,thyroid antibodies
- Vitamin D, B12
- Metabolic panel (fasting and post prandial glucose, insulin, HOMA score , HbA1c, lipid panel)
- Pregnancy test
- Colorectal cancer screening status check

IF SYMPTOMS PERSIST — INTEGRATIVE / FUNCTIONAL CONSIDERATIONS

- Comprehensive stool analysis, microbiome diversity, dysbiosis, H. pylori, Candida, inflammatory markers
- SIBO breath test, a frequent driver of bloating in perimenopausal women
- ? Expanded hormone panel, estrogen metabolism pathways, cortisol rhythm, progesterone?- Not recommended unless there is a question about menopause status , ex:, partial hysterectomy

VIGNETTE 1 · Jenny's Story

Stepwise Treatment — What to Address First

- **Correct any identified secondary cause**
- **Constipation: dietary fiber first line: begin soluble fiber (psyllium), titrate ~5 g/week with adequate hydration toward a 30 g/day of total fiber target, alongside physical activity**
- **Perimenopausal symptoms: hormone therapy when vasomotor symptoms (VMS)/bleeding are bothersome.**
    - **Primary indication is moderate-to-severe vasomotor symptoms; E+P because she has an intact uterus; start low, go slow: oral estradiol 0.5 mg/day or transdermal 0.025–0.0375 mg/week**
- **Still cycling with irregular bleeding: a combined hormonal contraceptive may be preferred over conventional MHT — it regulates bleeding, controls vasomotor symptoms, and provides contraception.**
- **ACOG and The Menopause Society endorse continuing hormonal contraception until age 55, absent contraindications**

DISCUSSION PROMPTS

- Which symptom is most bothersome to her?
- Is the constipation truly benign?
- What are her contraception needs?

Why Falling Estrogen Slows, and Sensitizes, the Gut

Motility & Bile — "The Unmasking Effect"

- Named for how hormonal instability worsens or unmasks previously subclinical gut issues — SIBO, histamine intolerance, mild dysbiosis
- Falling estrogen and progesterone slow smooth-muscle contraction → longer transit time, gas, constipation and distension
- Estrogen supports hepatic bile acid synthesis and secretion; its decline reduces bile's antimicrobial activity in the small intestine — raising SIBO risk

The Mast Cell-Histamine Connection

- Dips in progesterone and fluctuating estrogen destabilize mast cells, causing them to release excess histamine
- The gut houses the bulk of the immune system and is lined with mast cells: destabilization triggers gut cramping, bloating, and systemic symptoms (hives, headaches, anxiety, sleep-disrupting palpitations)
- Explains why women suddenly lose tolerance to alcohol and sulfur-rich foods (both high in histamines) during perimenopause

Vignette 2, Lisa

Doc, my reflux has been worse since I started MHT. Do I need a scope?

53-year-old established on combined estrogen–progesterone MHT for 18 months and doing well, except for this burning in the chest, throat and acid reflux.

VIGNETTE 2 · Lisa

MHT Can Cause GI Symptoms

OR 1.23

higher odds of new gastroparesis-type symptoms ≥30 days after starting HRT (78,192 users vs. 1,604,822 non-users), plus more nausea/vomiting, constipation, epigastric pain, distention, and more PPI/anti-emetic scripts and endoscopy referral

aOR 1.29

higher GERD odds with HT overall — but estrogen carries the risk, not progesterone: estrogen-only HRT raised GERD, erosive GERD, Barrett esophagus, and stricture; progesterone-only did not, in a large database study

- **Reflux-predominant: favor a lower estrogen dose, progesterone-sparing regimen, or progesterone-only where appropriate, and stay vigilant for complications**
- **New nausea/bloating/gastroparesis-type symptoms: reassess timing relative to MHT start; consider dose reduction or route change before adding chronic prokinetics/PPIs**
- **Remember the countervailing effect: HRT restores slower, premenopausal-range gastric emptying, it may help rapid-transit symptoms while worsening reflux**

HRT and the Gallbladder: Worth Owning as the GI Physician

1.74

relative risk of gallbladder disease with oral HRT, vs. 1.17 with transdermal : Million Women Study, >1 million women

1 in 140

cholecystectomies avoided over 5 years for every 140 women switched from oral to transdermal estrogen

- **Mechanism: oral estrogen increases biliary cholesterol saturation via first-pass hepatic action; transdermal lowers it**
- **Dose- and formulation-dependent : higher oral doses confer greater risk; oral conjugated equine estrogens carry slightly higher risk than oral estradiol**
- **Biliary tract cancer risk was roughly 2-fold higher with combined estrogen + progesterone, and higher still with oral route, topical preparations were null**
- **One outlier Korean cohort found the highest gallstone risk with topical estrogen; authors attributed this to selection bias (topical preferentially prescribed to higher-risk women)**

VIGNETTE 2 · Lisa

MHT and Reflux: What to Check Before You Reach for a PPI

MHT REGIMEN REVIEW

- MHT is a plausible contributor to new reflux, estrogen relaxes the lower esophageal sphincter via the nitric oxide pathway
- Can the estrogen dose or route be optimized?
- Is a more progestogen-dominant approach appropriate?

MEDICAL MANAGEMENT

When is a PPI appropriate? Reserve for confirmed/likely GERD after the regimen and lifestyle levers below have been considered.

Upper endoscopy? Risk factors?

OVERLAPPING GERD-AGGRAVATING FACTORS

Several factors that lower LES pressure overlap directly with menopause management:

- **Medications / UPF /Poor sleep / IBS mislabel**
- **Reducing high-fat meals**
- **Reducing alcohol and caffeine intake**
- **Progesterone itself**

EVIDENCE-SUPPORTED LIFESTYLE MEASURES

- Weight loss
- Avoid meals within 2–3 hours of bedtime
- Head-of-bed elevation for nocturnal symptoms
- Smoking cessation & trigger-food avoidance

Vignette 3, Sharon

Doc, my sister says I need MHT with my GLP-1?

48-year-old perimenopausal patient on a GLP-1 medication for BMI >30, sleep apnea and prediabetes HbA1c 5.9%, considering using MHT.

Vignette 3, Sharon

On a GLP-1 for Metabolic Syndrome, Considering MHT

PRESENTING FEATURES

- On a GLP-1 receptor agonist for insulin resistance (Tirzepatide 7.5 mg) x 8 months
- Considering adding MHT
- Mild vasomotor symptoms
- Mild GI sx-, mild nausea, early satiety? GLP-1
- Decrease in muscle strength, struggling with body composition
- Poor sleep, she is not consistent with CPAP
- Joint pain and frozen shoulder (limiting weight training)

DISCUSSION FRAME

- *GLP-1 indications considerations*
- *Exacerbation of menopausal symptoms*
- *Indication and selection of overlapping symptoms (GI side effects vs. menopausal symptoms)*
- *Importance of communication between prescribing providers.*

Vignette 3, Sharon

GLP-1 GI Effects vs. Perimenopausal Symptoms Overlapping Presentations

Symptom	Favors GLP-1 Cause	Favors Perimenopausal Cause
Nausea, vomiting, early satiety, bloating	Onset/worsening tracks with initiation or dose escalation; dose-dependent; improves on stable dose	Persistent, unrelated to titration
Constipation	Common (17–24%); temporally linked to GLP-1 dosing	Perimenopausal slowed transit; hypothyroidism; iron therapy
Fatigue, mood changes, hot flashes	Can appear if oral estrogen absorption dips during titration	Core vasomotor/mood features of perimenopause
Reflux / dyspepsia	Reported with GLP-1 delayed emptying	Estrogen effect on LES; primary GERD

Vignette 3, Sharon

GLP-1 + MHT: Compatible, But They Must Be Coordinated

GLP-1 therapy and MHT are compatible and complementary. The central issue is pharmacologic, not a contraindication.

- GLP-1-induced delayed gastric emptying can transiently reduce absorption of oral estrogen, route and timing of titration matter
- Diversity of microbiome changes during perimenopause compounds the picture: declining estrogen is already associated with reduced gut microbial diversity, a compositional shift toward a more “male-like” profile, and impairment of the estrobolome and gut-barrier support, with a possible increase in SIBO on GLP-1
- The double-hit of menopause: loss of estrogen’s insulin-sensitizing effect combined with a dysbiosis-driven drop in SCFA-producing bacteria accelerates insulin resistance and abdominal fat storage
- Overlapping GI/menopausal symptoms make attribution difficult and demand coordinated prescribing
- Slow, deliberate titration of GLP-1, GI side effects are dose-dependent and cluster at initiation and dose escalation

How Menopause Reshapes the Gut Microbiome

DEPLETED

- Butyrate-producing bacteria (e.g., Roseburia) ↓
- Microbial diversity (alpha diversity) ↓
- SCFA production ↓
- Akkermansia muciniphila altered — key species for gut-barrier & metabolic health
- Estrobolome GUS activity ↓

ENRICHED

- Bacteroidetes relative abundance ↑
- Prevotella species ↑
- Sutterella wadsworthensis ↑ — associated with elevated blood pressure
- Pro-inflammatory taxa ↑

HCHS/SOL metagenomic study (2,300 participants : 295 premenopausal, 1,027 postmenopausal) confirmed this pattern and additionally found depleted Clostridium lactatifermentans, which is strongly associated with a higher waist circumference and greater metabolic-syndrome risk.

This is exactly the dysbiosis pattern driving the insulin-resistance and weight side of the GLP-1 conversation.

Case in Point: Initiating MHT Alongside GLP-1 Therapy

48-year-old perimenopausal woman on a GLP-1 (tirzepatide) for metabolic syndrome — vasomotor symptoms, poor sleep, body composition changes, and joint pain/frozen shoulder limiting resistance training

GLP-1 Titration (Tirzepatide)

- Start Tirzepatide 2.5 mg SQ q week
- Hold dose through month 1. No early increase
- If losing 1–2 lb/week or ≥1% body weight, stay at that dose to minimize side effects
- Reassess trajectory before advancing the dose

Objective Monitoring & Mindset

- DEXA at baseline + every 3–6 months. Fat, lean mass, bone density
- BIA monthly in-office or daily at home; grip strength as a muscle-function proxy
- Waist-to-hip ratio, waist circumference, and other objective metrics
- Expect day-to-day scale shifts from water. Don't over-interpret
- Protein: 1.2–1.5 g/kg/day (up to 2.0 g/kg while actively losing)
- Decouple mindset from the scale; prioritize behavioral change

MHT Initiation (Transdermal E + P)

- Transdermal estradiol + progesterone, combined regimen
- Unopposed estrogen for ~3 months, then add progesterone
- Targets vasomotor symptoms, sleep, and body composition support
- May help joint symptoms limiting resistance training. Consider PT referral.

The 1–2 lb/week (~1% body weight) titration pace reflects a common precision-titration practice pattern, not an FDA-labeled threshold. The tirzepatide label leaves pacing to clinical judgment.

Vignette 3, Sharon

Communication Between Prescribers

Reconcile medications

Flag absorption-sensitive oral agents before GLP-1 initiation or up-titration, adjusting timing as needed

Share the titration schedule

So the MHT prescriber anticipates possible transient VMS breakthrough

Agree on who monitors what

Explicit ownership prevents symptoms from falling through the cracks

Counsel the patient as the connective tissue

She is often the only person talking to every prescriber — equip her to relay changes

Vignette 4, Rochelle

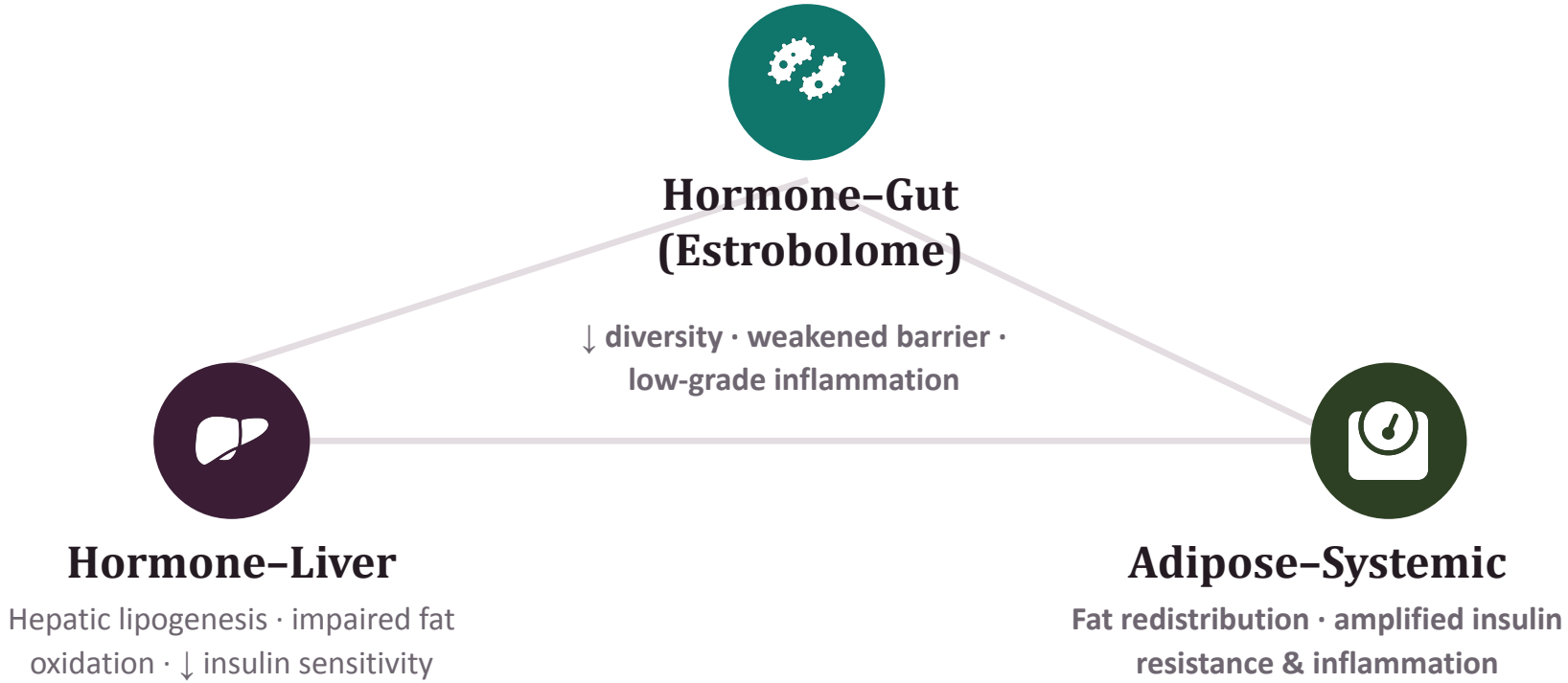
“Doc, I was just diagnosed with diabetes, my liver numbers are high, and I’m gaining weight. I feel tired, anxious and irritable all the time. I think it's all hormones.”

A 52-year-old woman with fatigue, weight change, and new diagnosis diabetes, HbA1c 7.6%, fatty liver, elevated BP and triglycerides, reporting significant psychological symptoms.

Vignette 4, Rochelle

The Gut-Liver-Hormone Axis

Estradiol is a master regulator that normally amplifies insulin, leptin, and GLP-1 sensitivity and dampens ghrelin. Its withdrawal in the menopausal transition removes this coordinating signal — the unifying mechanism disrupting metabolic homeostasis.



Vignette 4, Rochelle

GYN, Menopause Lens

PRESENTING FEATURES

- Diabetes
- Weight change
- Early metabolic-syndrome markers
- Fatigue
- Irritability and anxiety

PRIORITY SEQUENCING — WHAT TO ADDRESS FIRST

1. Confirm menopause stage & characterize symptoms.
Document cycle pattern, VMS severity, sleep disruption, and genitourinary symptoms; Screen thyroid (TSH, free T4) and anemia (CBC) as independent, treatable causes of fatigue.

2. Treat diabetes + NAFLD together.
Start a GLP-1 RA + plus structured lifestyle change (Mediterranean diet, exercise); target ≥ 5–10% weight loss.

3. Stage the liver; control CV risk.
FIB-4 → VCTE/ELF; refer to GI. Control BP and triglycerides.

4. Evaluate mood on its own merits.
Formal mood evaluation; treat with CBT ± SSRI/SNRI.

5. Reassess menopausal symptoms.
If bothersome VMS persist and CV risk factors are controlled, consider transdermal MHT via shared decision-making.

From Labs to Lifestyle: A Case-Based Treatment Approach

52-year-old woman presenting with fatigue, weight change, newly diagnosed Type 2 DM (HbA1c 7.6%), NAFLD, elevated triglycerides

Nutritional Foundation

- Reduce alcohol intake
- Move away from processed, sedentary eating patterns
- Shift toward whole, anti-inflammatory foods
- Ensure adequate fiber intake

Consistent Eating Pattern

- Scheduled eating throughout the day
- Supports glycemic balance
- Buffers cortisol-driven glucose shifts
- Especially relevant given perimenopausal hormonal shifts

Collaborative, Whole-Person Care

- Refer to a dietitian for an individualized plan
- Refer to GI, given fatty liver and the gut-hormone connection
- Refer to GYN to integrate hormonal status into metabolic care
- A coordinated team beats isolated specialists

Vignette 4, Rochelle · GI Lens

Metabolic & Motility Workup

- Diabetes — screen and monitor as part of the GI workup
- Micronutrient evaluation
- Motility issues: gastroparesis, GERD, constipation
- Insulin resistance: fasting insulin/HOMA-IR as part of the metabolic workup — often missed once a diabetes diagnosis is already in hand
- Gut contribution: dysbiosis and reduced SCFA-producing bacteria blunt GLP-1-mediated insulin sensitivity (see the Vignette 4 mechanism slide)

Hepatobiliary & Hormone Levers

- MASLD — assess degree of fibrosis
- Gallbladder disease
- Mode of administration of MHT: bypass the liver, or transdermal?
- MASLD and type 2 diabetes are bidirectional — fibrosis stage should inform diabetes risk stratification, not just liver-specific follow-up
- Loss of estrogen's insulin-sensitizing effect compounds hepatic insulin resistance — the mechanistic reason gut-liver-hormone status belongs in the diabetes workup

HRT and the Gut: What the Evidence Shows

Microbiome & Barrier Evidence

- Systemic transdermal estradiol bypasses first-pass liver metabolism — stable levels, no added hepatic burden
- MHT supports re-diversification of the gut microbiota, helping reverse the low-diversity pattern seen postmenopause
- Low-dose vaginal estrogen is the gold standard for GSM — re-feeds Lactobacillus, lowers vaginal pH, cuts recurrent UTIs by ~50%

Insulin Resistance & Diabetes

- 2025 meta-analysis: HT improves insulin-resistance markers in non-diabetic postmenopausal women (Li et al., Climacteric 2025)
- Menopause and diabetes risk are mechanistically linked, not just comorbid (Lambrinoudaki et al., 2022)
- Estrogen is a natural insulin sensitizer — its loss, plus dysbiosis-driven SCFA decline, is the “double hit” behind cases like Rochelle's
- Route matters too: oral's glycemic edge must be weighed against hepatobiliary risk in MASLD/gallbladder patients

Route and dose choices for MHT are not just symptom control, they are microbiome and gut-barrier decisions.

Black Women & the Menopause Transition: What SWAN Shows Us

Data drawn from the Study of Women's Health Across the Nation (SWAN)

Vasomotor symptoms hit harder and longer

~50% more likely than White women to report hot flashes/night sweats; median VMS duration ~10 years vs. ~6.5 years.

The earlier transition is mostly not biology

Final period ~8–9 months earlier on average — mostly explained by socioeconomic and health factors, not race itself.

f.

Sleep is worse than self-report suggests

Objective actigraphy/polysomnography shows shorter sleep duration, more awakenings, less deep sleep than patients report.

Depressive symptoms: more common, treated less

Higher rates of clinically significant depressive symptoms and incident depression, but lower rates of psychotherapy and medication

.

Cardiometabolic risk starts disproportionately high

Higher baseline obesity, hypertension, diabetes, and metabolic syndrome compound menopause-related CV risk; hypertension more often untreated.

HT use is lower despite greater symptom burden

SWAN data: Black women are about half as likely as White women to use hormone therapy for symptom relief.

Everyday discrimination is a measurable clinical variable, not just context — SWAN links chronic discrimination and stress to elevated allostatic load, worse sleep, and longer VMS duration.

BRINGING IT TOGETHER

Monday-Ready Protocols

Practical, evidence-informed levers you can use across all four vignettes, starting this week!

KEY TAKEAWAYS

Eight Things to Carry Into Your Next Clinic Day

1. **HRT can cause GI symptoms, not just fix them** — estrogen (not progesterone) drives new reflux; titrate MHT by formulation and route, not just dose.
2. **Treat menopause as a whole-body, microbial transition** — not an isolated hormonal event. See the whole patient, break the silos, and support the microbiome as a non-hormonal pillar of care.
3. **Gut-barrier permeability rises 2–2.5 years before the final period** — early perimenopausal support matters, not just post-menopausal damage control.
4. **Start with the foundation, every time** — fiber, sleep hygiene, movement, and stress-reduction belong in every treatment plan, not as an afterthought to MHT.
5. **Personalize and sequence, don't stack** — titrate MHT choice, dose, and route to the individual's clinical picture, and treat what's most bothersome, dangerous, or reversible first.
6. **Route and progestogen choice are gut decisions too** — transdermal estradiol lowers gallbladder/NAFLD risk, and micronized progesterone preserves estrogen's metabolic benefit without added VTE risk.
7. **Build your care team and measure objectively** — identify 2–3 trusted providers across PCP, GI & GYN, and track symptoms with a validated tool like the Greene Climacteric Scale rather than impression alone.
8. **Don't anchor on menopause — meet patients where they are** — stay alert to bias, keep standard screening on schedule, and offer culturally sensitive, evidence-based non-hormonal alternatives (e.g., Femmenessence) when a patient's background shapes her comfort with HRT/MHT.

Referral Criteria: When the Workup Exceeds Primary Scope

Refer to GI

- Alarm features: rectal bleeding, unintentional weight loss, iron-deficiency anemia, nocturnal symptoms
- Severe dysmotility gastroparesis, constipation,
- Unexplained micronutrient deficiency- low iron
- Family history of colorectal cancer or IBD, or onset of new GI symptoms after age 45–50
- Age-appropriate colorectal cancer screening not yet up to date
- Abnormal LFTs or suspected fatty liver disease beyond lifestyle-responsive dysbiosis

Refer to GYN-Menopause / Endocrinology

- HRT dosing/route optimization needed beyond primary comfort
- Complex GLP-1 / HRT interaction requiring coordinated titration
- Diagnostic uncertainty, perimenopause vs. thyroid or other endocrine disease

Where digestive enzymes like FODZYME® fit in

Fructan hydrolase, alpha-galactosidase, lactase

Increased FODMAP sensitivity

Can be due to increased visceral hypersensitivity, increased intestinal permeability, and changes in the gut microbiome.

Slowed gut motility

Enzyme therapy can reduce gas production from FODMAPs and reduce the amount of gas that can get trapped behind stool.

To eat more fiber-rich foods

If there are any known or suspected FODMAP sensitivities present, enzymes can help avoid restriction, build tolerance, and support symptoms.

FODMAP Substrate	Common Foods	Active Enzyme
Fructan (inulin, FOS, levan, graminan)	Onions, garlic, scallion, shallot, leek, wheat, artichoke, Brussels sprouts, dried fruit, beets	Fructan hydrolase
Galactooligo-saccharides (GOS)	Beans, lentils, chickpeas, soymilk, soft tofu, peas, cashews, pistachios, almond meal	Alpha-galactosidase
Lactose	Milk, ice cream, soft cheeses yogurt, kefir, pudding, custard, condensed milk	Lactase

In Vitro Evidence: Targeted Enzymatic Digestion

Castro Ochoa K, et al. In Vitro Efficacy of Targeted FODMAP Enzymatic Digestion in a High-Fidelity Simulated GI Environment. Gastro Hep Advances. 2023. doi:10.1016/j.gastha.2022.10.011

90%

of fructans degraded within 30 minutes in a validated SHIME® simulated gut model

≈70%

of released fructose absorbed during simulated small-intestinal transit, limiting substrate reaching the colon

SCFA & Butyrate Preserved

microbial gas production decreased while short-chain fatty acid production was substantially maintained

Why this matters clinically

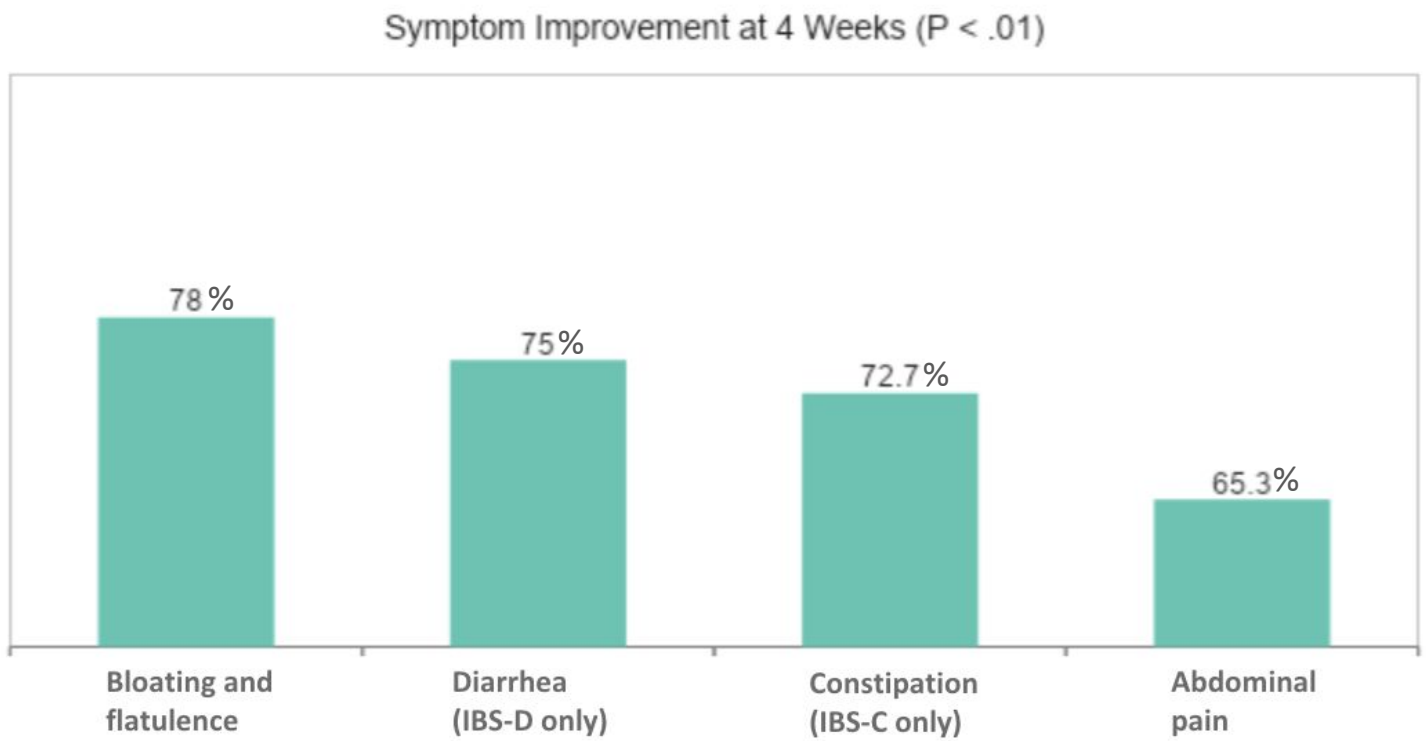
A strict low-FODMAP diet depletes the fermentable substrate the microbiome needs to produce SCFAs, including butyrate. This in vitro model suggests targeted enzymatic digestion can reduce the gas-producing fermentation burden while preserving that substrate — a mechanism, not yet a clinical outcome.

Laboratory (SHIME®) model — industry-funded (Kiwi Biosciences). Establishes plausibility, not patient outcomes.

Real-World Evidence: A 4-Week Enzyme Cohort Study

Kaye AJ, et al. FODMAP-Targeting Digestive Enzyme Blend for Management of GI Symptoms: A "Real-World" Pre-Post Intervention Cohort Study. Gastro Hep Advances. 2026. doi:10.1016/j.gastha.2026.100898

Design: prospective, single-arm, open-label, pre-post cohort · n = 118 · 4 weeks · IRB-approved, independently analyzed



Also significantly improved (P < .01):

Quality of Life · Mental Well-Being · Food Avoidance Behaviors

Reading the evidence honestly

Open-label, single-arm, self-reported, industry-funded (Kiwi Biosciences). A promising real-world signal that warrants controlled follow-up — not a replacement for individualized assessment.

Supplements for Menopausal Symptoms: Evidence & Safety

Supplement	Evidence for Menopausal Symptoms	Key Safety Caveats	Refs
Soy isoflavones (dietary/extract)	Best-supported: meta-analysis shows modest reduction in daily hot flashes and vaginal dryness (not night sweats)	Estrogenic activity — theoretical concern for endometrial hyperplasia/estrogen-sensitive cancers	[5]
Red clover (isoflavones)	Mixed: no effect on hot flash frequency; one study showed reduced night sweats	Same phytoestrogen concerns as soy	[5]
Evening primrose oil	No benefit over placebo in higher-quality trials; one small RCT showed modest severity improvement only	GI upset; bleeding risk, caution with anticoagulants	[1, 4, 6]
Maca (Lepidium meyenii)	Limited, low-quality data; a few small RCTs suggest benefit on climacteric scores/mood, but too fow and too small for firm conclusions	Generally well tolerated; long-term safety not established	[1-2, 7]
Black cohosh	No significant effect on hot flashes in meta-analysis; data conflicting	Reports of hepatotoxicity/liver injury	[1, 3, 5]
Flaxseed (lignans)	Inconsistent; some studies show reduction, others no difference	Generally safe	[5, 8]
Rhubarb extract (ERr 731, Rheum rhaponticum)	ERβ-selective; several RCTs report improved hot flashes and quality of life with favorable safety	Longer-term data limited	[8-9]
Ginseng, ginkgo biloba	Not superior to placebo for vasomotor symptoms	Bleeding risk (ginkgo)	[3]
Vitamin E / omega-3	Minimal; combined use may modestly lower hot flash intensity	Generally safe	[1, 8]
Probiotics	Poor/inconsistent evidence for vasomotor symptoms	Generally safe	[4, 8]
Curcumin	Preliminary — one trial showed reduced hot flashes at 4 weeks	Generally safe	[8]

Route of Administration: Same Hormone, Different Physiology

Oral estrogen undergoes hepatic first-pass metabolism; transdermal bypasses it. That single difference explains a consistent trade-off.

Outcome	Oral estrogen	Transdermal estradiol	Preferred route
Gallbladder disease	Substantially increased (RR ~1.7)	Modestly increased (RR ~1.2)	**Transdermal**
Biliary tract cancer	Increased	Null (topical)	**Transdermal**
T2DM / insulin resistance	Greater reduction	Reduction, weaker	**Oral (glycemia)**
Triglycerides	Increased	Neutral	**Transdermal**
MASLD	May worsen	Neutral / favorable	**Transdermal**
LDL / HDL cholesterol	More favorable	Neutral	**Oral (LDL/HDL)**
VTE / stroke	Higher	Lower	**Transdermal**
GI motility / microbiome	No comparative data	No comparative data	No difference established

When your patient needs more support in midlife

Dr. Terri Malcolm
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Dr. Vivian Asamoah

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Dr. Vivian Asamoah, MD, IFMCP

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Thank You

Questions & Discussion

Dr. Vivian Asamoah, MD, FACG, IFMCP
Gastroenterology, Hepatology & Nutrition
Integrative & Functional Medicine

Dr. Terri Malcolm, MD, FACOG, MSCP
Obstetrics & Gynecology
Certified Menopause Specialist

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