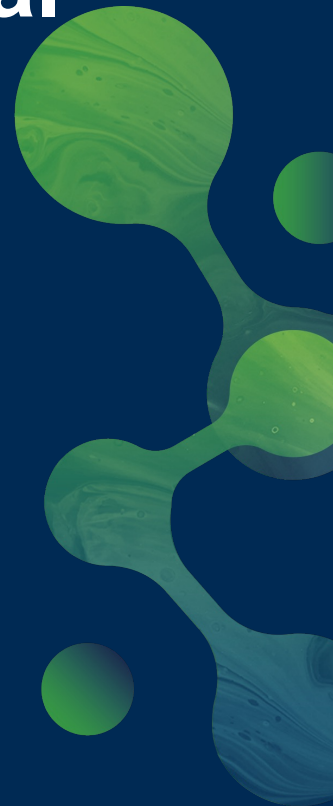




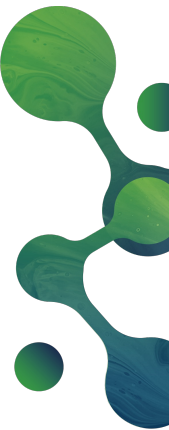
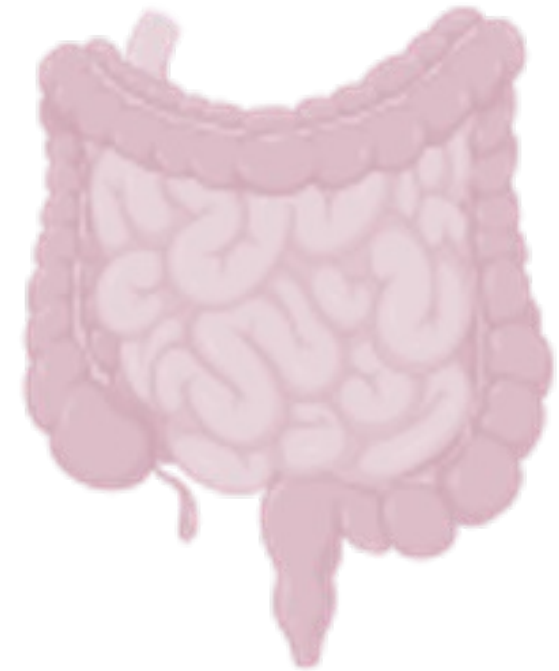
Menopause and the Microbiome: Clinical Strategies for Restoring Digestive and Metabolic Health

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AGENDA

- Impact of hormonal decline
- Importance of the gut microbiome
- Key changes at Menopause
- Vaginal – Gut Axis
- The estrobolome
- Fibre, PHGG & Polyphenols
- Use of probiotics



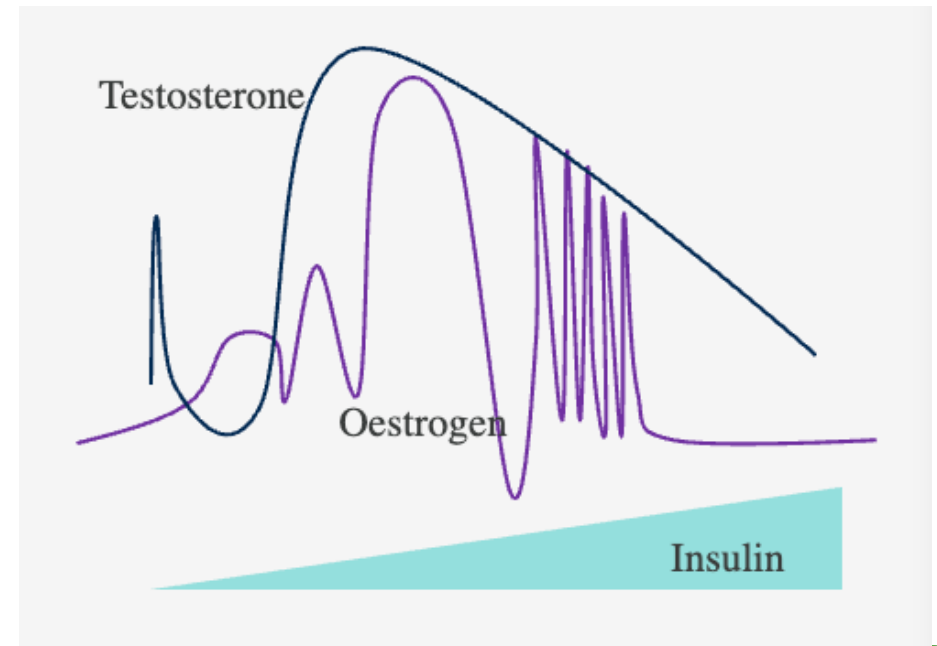
Impact of Hormone Decline

Oestradiol and progesterone are **systemic regulators**.

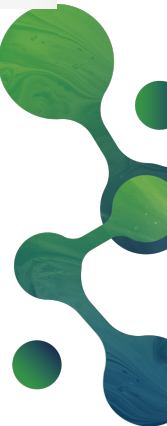
Receptors expressed throughout the body **including the gut**.

As they decline during menopause, **gut structure, function, and microbial balance are directly affected**.

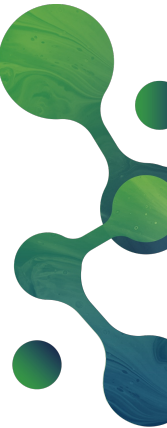
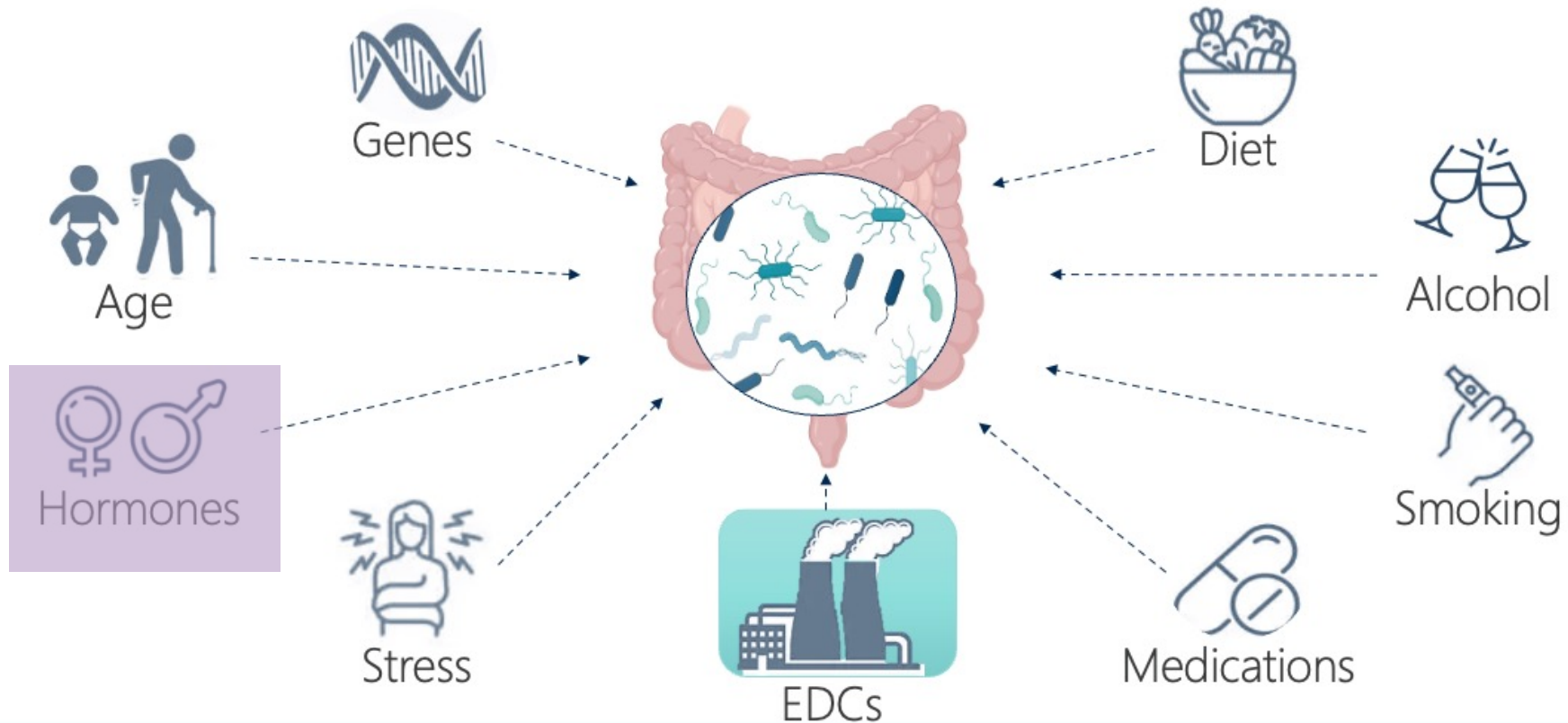
Because the gut influences immune, metabolic, and neuroendocrine systems, it becomes a **central mediator of whole-body health during menopause**.

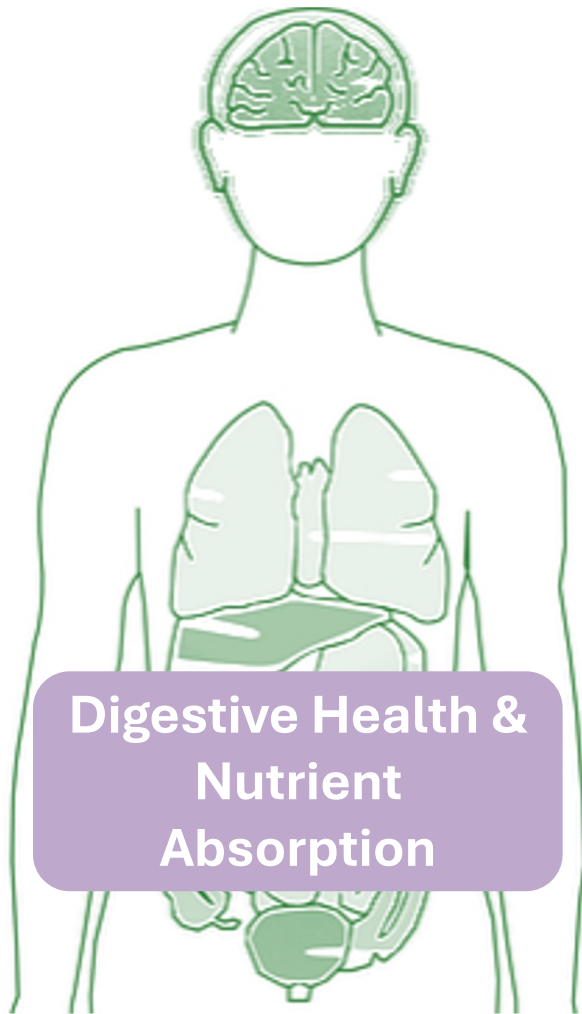


Gut changes may contribute to increased risk of metabolic, cardiovascular, and bone diseases in postmenopausal women. It may also contribute to cognitive and mood changes



Factors altering gut microbiota





Importance of the Gut Microbiome at Menopause

Cardiometabolic Health, weight
NAFLD

Vaginal Health

Gut-Skin Axis
Oral Microbiome

Bone- Gut Axis
Gut-Muscle Axis

Digestive Health &
Nutrient
Absorption

Circadian Rhythm &
Sleep Regulation

Immune
Modulation /
inflammation

Brain-gut
communication

Oestrogen
Metabolism



Common Gut Symptoms at Menopause

- Bloating / abdominal distension
- Constipation
- IBS symptoms
- Reflux
- Abdominal pain
- Incomplete evacuation

DRIVEN BY

Hormonal decline
Pelvic floor weakening
(mechanical defecatory dysfunction)
Shift to The "M-Type"
Microbiome
Microbial dysbiosis
Reduced SCFA production
Increased gut permeability
Altered serotonin signaling
Stress and sleep disruption

Hormone Decline & Age Influence: Diversity

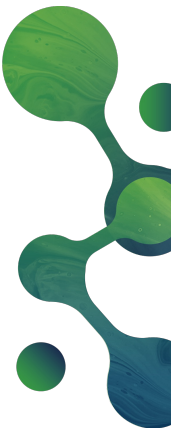
AGE

- Overall diversity tends to plateau midlife
- Key compositional shifts begin (↓ Bifidobacterium, ↓ SCFA producers)
- Less resilience to stressors

MENOPAUSE

- Reduced overall microbial richness
- Microbiome becomes more similar to male profile
- Reduced estrobolome potential
- Lower resilience to dietary and metabolic stress

Reduced **diversity** associated with insulin resistance, inflammation, cardiometabolic risk



Shift Toward a Pro-inflammatory Microbiome

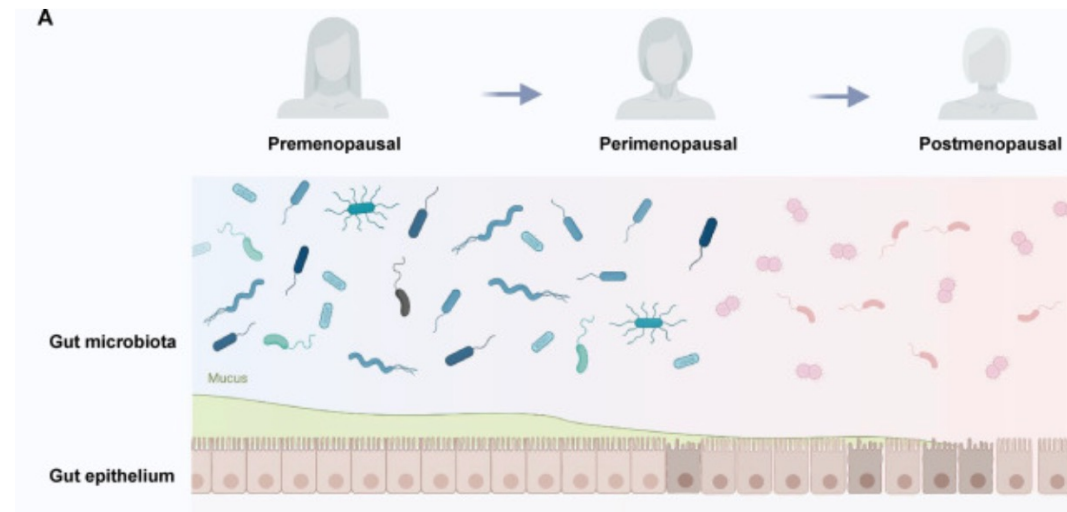
- ↓ Lactobacillus, Bifidobacterium,
- ↓ Akkermansia muciniphila
- ↓ Faecalibacterium,
- ↑ Proteobacteria (in women with higher VAT)

Increased endotoxin load

Altered estrobolome activity

Disrupted bile acid signaling

Altered Firmicutes:Bacteroidetes ratio



Yu et al. J. Genet. Genomics. 2025; 52(5):601-614.

Reduced Barrier Integrity

Across the menopausal transition:

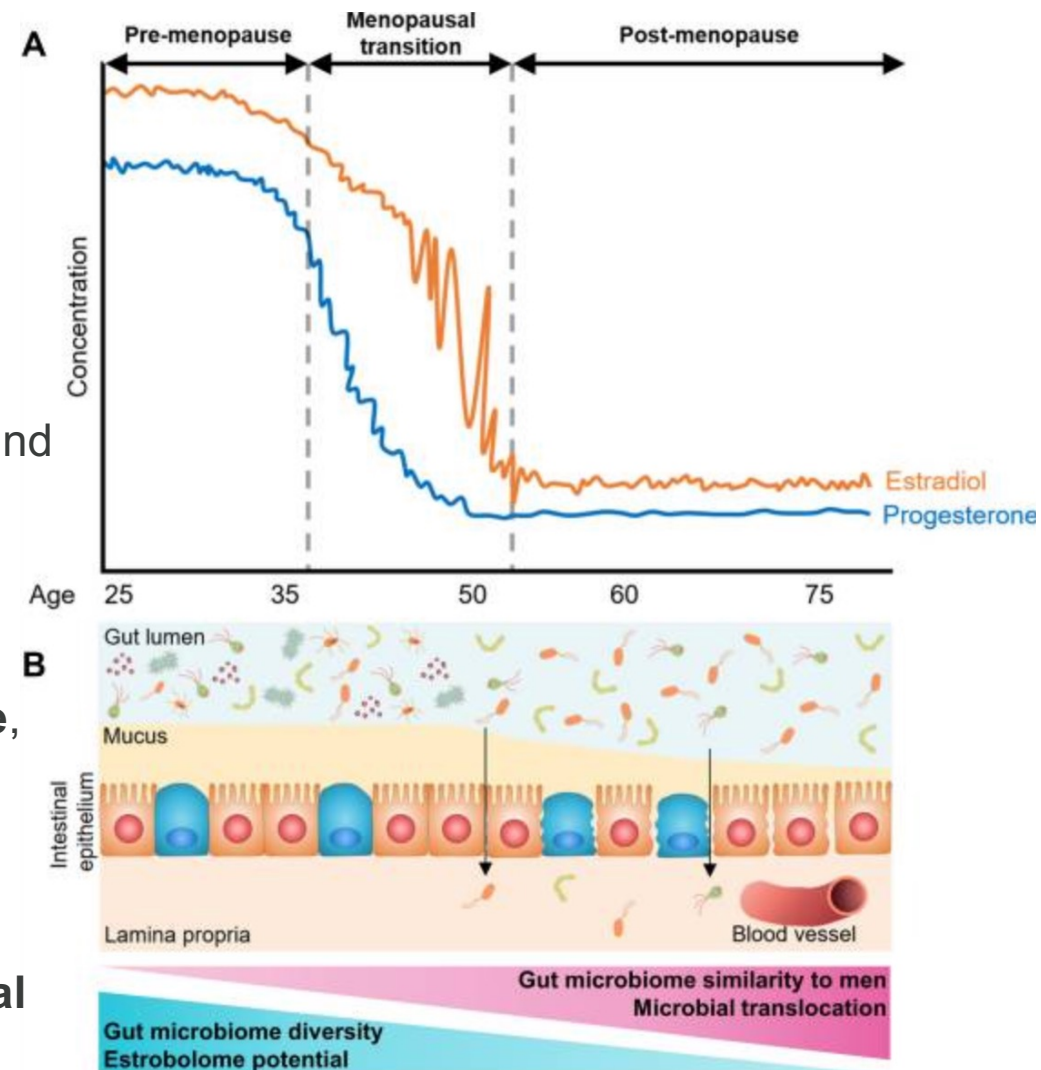
- ↑ Intestinal permeability
- ↑ Plasma IFABP (intestinal fatty acid binding protein – epithelial damage marker)
- ↑ LBP and sCD14 (markers of microbial translocation and immune activation)
- ↑ Circulating LPS (endotoxin)

The SWAN cohort data (Shieh et al.) showed that permeability **increases from pre- to post-menopause**, and is associated with:

Higher systemic inflammation (CRP)

Lower bone density

This suggests menopause is associated with **functional weakening of the epithelial barrier**.



Shieh et al JCI Insight. 2020 Jan 30;5(2):e134092
Peters et al. 2022 Int J Womens Health..

What Causes These Barrier Changes?

Loss of Sex Hormone Barrier Protection

Oestradiol / progesterone
Upregulate tight junction proteins
Stimulate mucin production
Enhance epithelial repair
Suppress NF-κB
Limit microbial translocation

This is a direct epithelial effect, independent of microbiome shifts.

Reduced SCFA (due to microbial shifts)

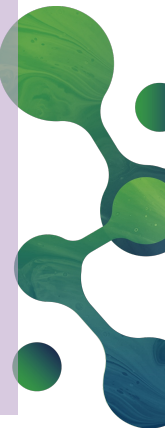
Butyrate increases:

- ✓ Occludin, claudins, ZO-1
- ✓ Enhances mucin (MUC2)
- ✓ Fuels colonocytes
- ✓ Suppresses NF-κB
- ✓ Promotes Tregs

Decline impacts barrier and inflammation

Secondary Amplifiers

- HPA axis activation (stress)
- Sleep/circadian disruption
- Visceral adiposity and endotoxemia
- Altered bile acid signaling
- Diet, alcohol, NSAIDs



SCFA & Systemic Impact

Butyrate acts via two mechanisms:

1. Local (gut barrier)

Tight junction, mucin, colonocyte energy, Treg induction, NF-κB suppression

2. Systemic signalling

GPR43 on L cells → ↓ GLP-1 & PYY release

GPR41/43/109A on immune cells & adipocytes → ↓ anti-inflammatory signalling

HDAC inhibition → epigenetic suppression of IL-6, TNF-α lost



↓ SCFA signalling contributes to:

Insulin resistance

Visceral adiposity

Bone resorption

Cardiometabolic risk

Sarcopenia risk (↓ mTOR/AMPK signalling)

The mechanism: LPS enters circulation → TLR4 activation → IL-6, TNF-α production

Gut-Brain Axis: Tryptophan Metabolism & Menopause

Altered pathway	Symptoms
Altered serotonin signalling in gut	Altered motility — constipation or diarrhoea
↓ Serotonin in CNS	Low mood, poor sleep, fatigue
↑ Quinolinic acid → NMDA activation	Heightened pain sensitivity, central sensitisation
↑ Neuroinflammation	Cognitive fog, anxiety, poor concentration
↓ Melatonin (downstream of serotonin)	Sleep disturbance

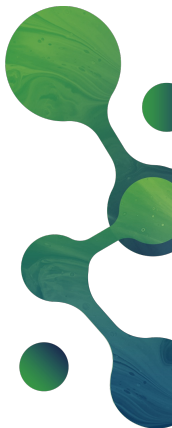
CLINICAL SUPPORT

Reduce IDO activation: Omega-3, polyphenols, Mediterranean diet

Repair gut barrier (*removes IDO trigger*):
Glutamine, zinc, vitamin D, curcumin, butyrate-producing fibres

Restore serotonin synthesis cofactors: B6, iron, magnesium, riboflavin (B2)

Support microbiome diversity (prebiotics, probiotics, plant diversity)
e.g Lactobacillus reuteri, Bifidobacterium infantis, Lactobacillus casei

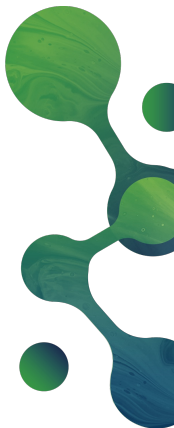


Menopause, Metabolic Health, and the Gut Microbiome

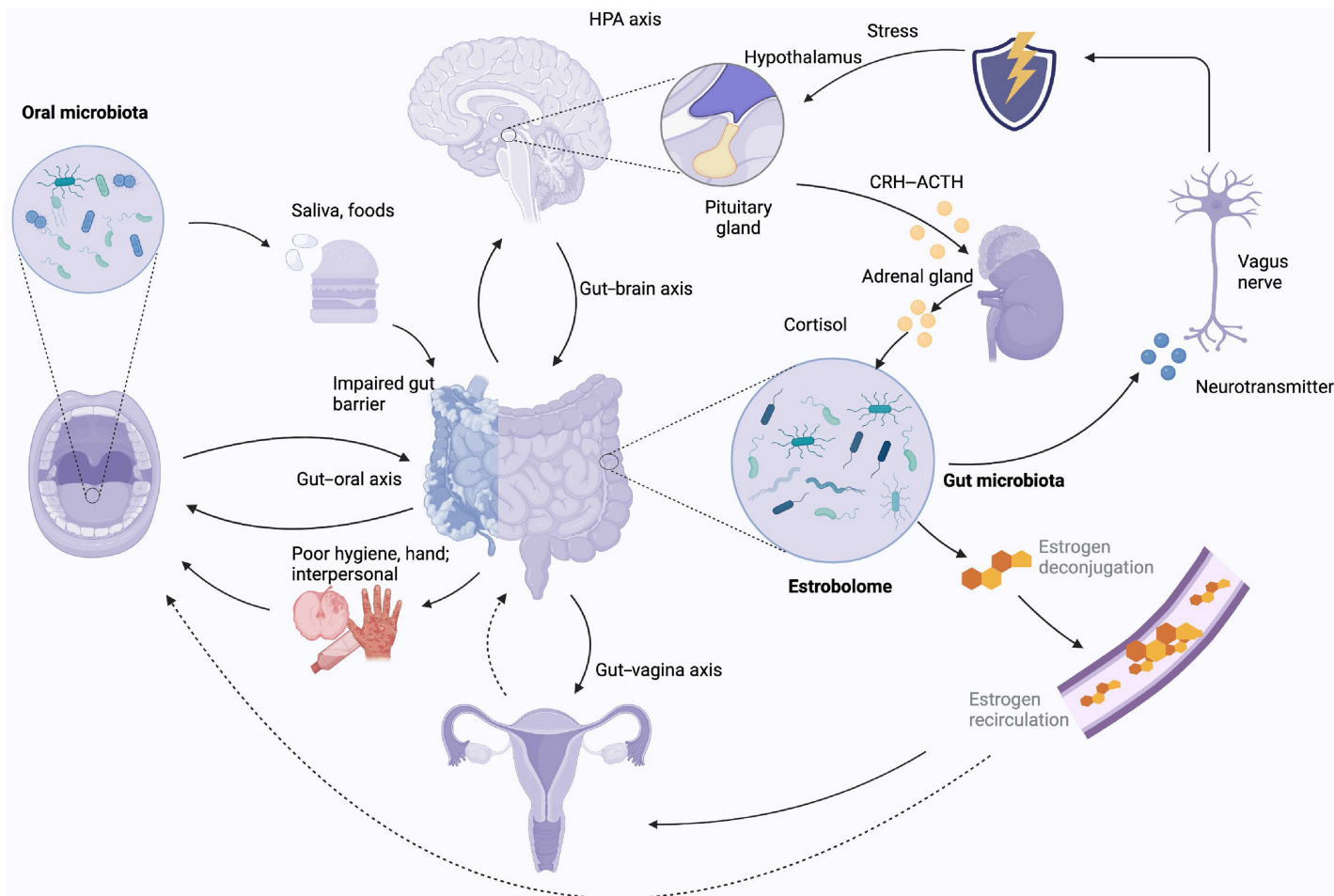
Gut microbiome shifts may **mediate or exacerbate** metabolic changes.

Gut Mechanism	Changes	Effect on Weight/Metabolism
Gut Permeability	Dysbiosis increases intestinal permeability	LPS endotoxins enter circulation → low-grade inflammation → visceral fat deposition; contributes to insulin resistance and metabolic syndrome
SCFA Production (Butyrate, Propionate, Acetate)	Reduced fiber fermentation → lower SCFAs	Impaired energy regulation, fat oxidation, appetite control; SCFAs regulate GLP-1, PYY, and other metabolic hormones
Inflammation / Metabolic Endotoxemia	Chronic low-grade inflammation from LPS	Insulin resistance, altered adipocyte function, visceral fat accumulation; amplifies metabolic risk during menopause
Microbial Diversity	Overall bacterial diversity decreases; loss of beneficial species (e.g., Faecalibacterium, Roseburia)	Lower SCFA production → impaired insulin sensitivity, reduced satiety signaling, altered energy balance; butyrate producers are key for metabolic health
Lifestyle & Age Interactions	Low fiber, sedentary lifestyle, aging immune system	Exacerbates dysbiosis and metabolic changes; modifiable factors can partially offset menopause-associated risk

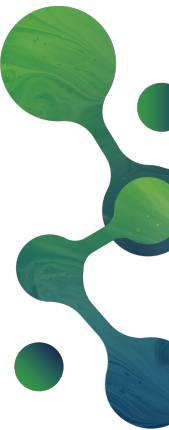
Other contributory factors may include Gut-Brain Axis / Appetite Signalling, Bile Acid Metabolism and estrobolome activity



Microbiome axes during menopause



The microbiome axes between the gut and brain, between the gut and vagina, and between the gut and oral cavity show bidirectional interaction that can impact both distant and local locations and impact health and quality of life of menopausal women



Menopause-related changes in bile acid metabolism

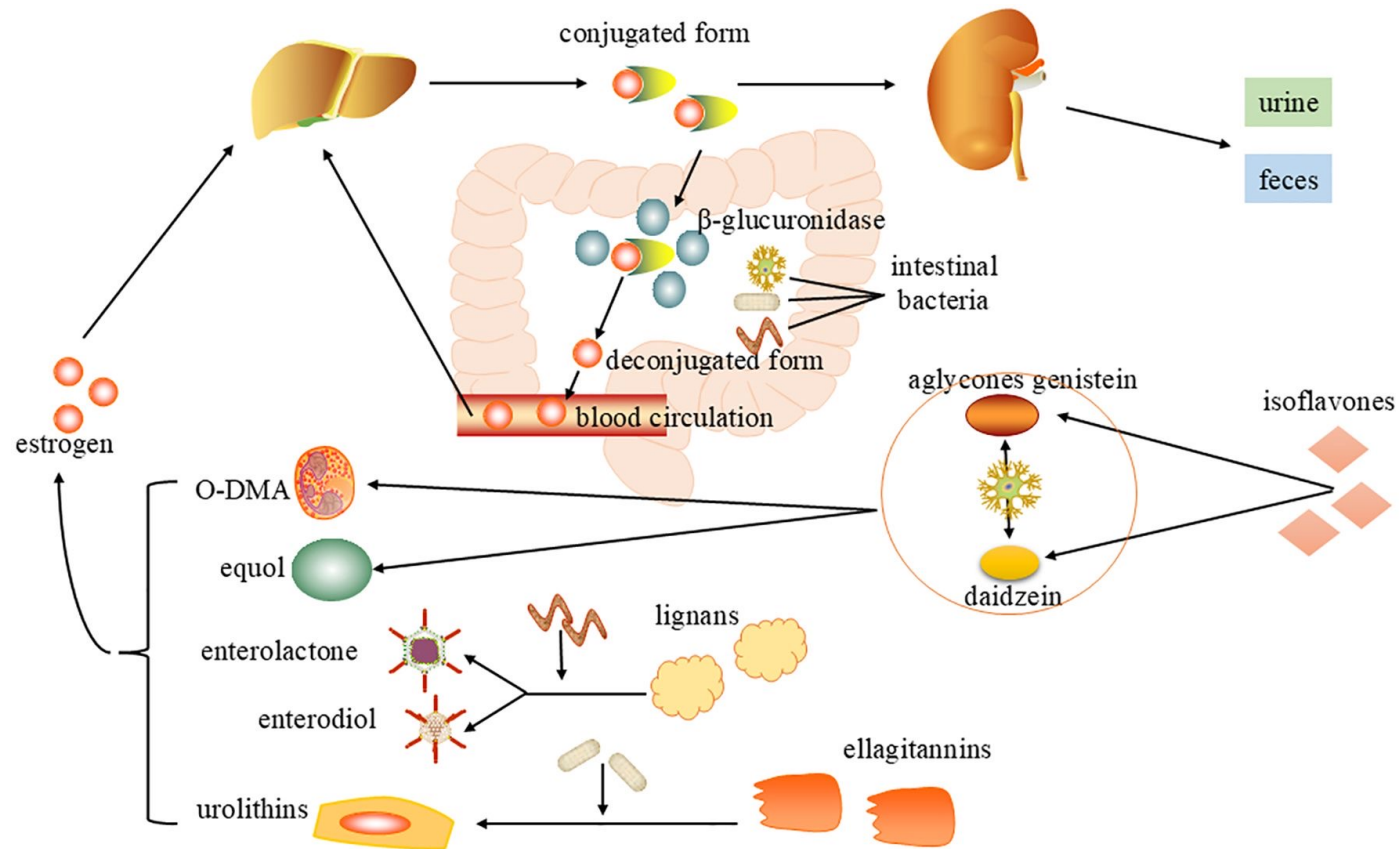
⚠️ Note: Mechanistic pathways largely inferred from metabolic disease literature; menopause-specific human RCT data remain limited.

Change	What happens	Clinical consequence
Bile acid synthesis (liver)	Declining oestrogen impairs FXR/LXR/SHP signalling → reduced synthesis efficiency	↑ LDL cholesterol Cardiovascular risk
Primary → secondary conversion (gut)	Gut dysbiosis reduces microbial conversion of CA/CDCA → DCA/LCA	Irregular secondary bile acid availability → impaired metabolic + immune signalling Glucose regulation
FXR–FGF19 feedback loop	Reduced intestinal FXR activation → lower circulating FGF19	Weakened bile acid synthesis feedback; disrupted lipid + glucose metabolism Metabolic liver disease
TGR5 signalling	Fewer secondary bile acids (DCA, LCA) to activate TGR5	↓ Energy expenditure, ↓ thermogenesis, weakened NF-κB suppression (preclinical) Inflammation · weight gain
Bile acid conjugation	Pool shifts toward glycine-conjugated forms; fewer taurine-conjugated acids	Taurine-conjugated forms more effective at receptor signalling (emerging evidence) Digestive symptoms
Bone signalling (animal data only)	Reduced TGR5/FXR removes inhibitory signals on osteoclast activity	Accelerated bone loss post-menopause Bone health

The Estrobolome

The **estrobolome** refers to the **collection of gut microbial genes** (and the enzymes they encode) that are involved in **metabolizing oestrogens**, most notably through **β -glucuronidase (GUS) and sulfatase enzyme activity**.

These enzymes **deconjugate (reactivate)** oestrogen conjugates excreted into the gut, allowing them to be **reabsorbed back into circulation via enterohepatic recycling**, thereby influencing systemic oestrogen levels.



The Menopause–Estrobolome Axis: A Breakdown in Recycling?

Menopause shifts the gut microbiome

Menopause is associated with reduced microbial diversity and altered estrobolome composition/function (Wang 2025).

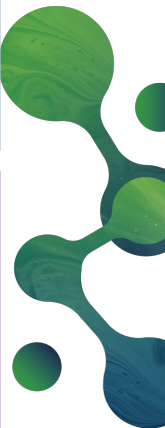
Reduced oestrogen recycling

Lower β -glucuronidase activity associated with decreased deconjugation and enterohepatic recycling, increasing faecal oestrogen loss and potentially further lowering circulating levels.

The gut as a modifiable regulator

Estrobolome changes intersect with bone, metabolic, and inflammatory pathways - both insufficient and excessive GUS activity may be unfavourable

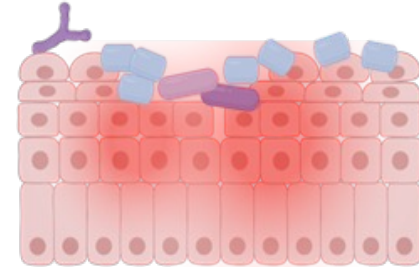
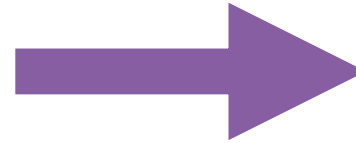
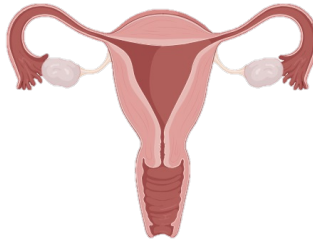
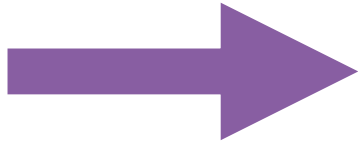
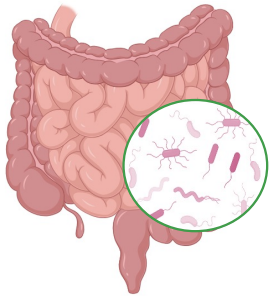
Clinical Goal: Support a balanced estrobolome via fibre diversity, polyphenols, and targeted probiotics to maintain physiological oestrogen recycling. Key strains with direct GUS/estrobolome evidence: *Levilactobacillus brevis* KABP052 (RCT data in peri/postmenopausal women); *Lacticaseibacillus rhamnosus* (selected strains show GUS activity in vitro).



Probiotics for Vaginal Health: *L. rhamnosus* GR-1 & *L. reuteri* RC-14.

Gut-vaginal crosstalk

Genitourinary Syndrome of Menopause (GSM), increased susceptibility to Bacterial Vaginosis (BV) and UTIs



Hypoestrogenism

- ↓ microbial diversity
- ↑ dysbiosis
- ↑ inflammation
- Gut barrier dysfunction
- Reduced estrobolome

Vaginal ecosystem

- Reduced Vaginal Glycogen.
- ↑ vaginal pH
- ↑ leukocyte infiltration
- "Atrophic Epithelium" (Thinning)

Dysbiosis

- ↓ *Lactobacillus* dominance
- ↑ *Prevotella*, *Mycoplasma*, *Gardnerella*

HRT – Vaginal Microbiome

HRT, especially Oestrogen, tends to restore vaginal microbiome “homeostasis.”

Oestrogen (especially vaginal oestrogen):

Restores glycogen

Promotes Lactobacillus dominance

Reduces diversity back to a low-diversity, stable state

In the vagina, **HRT-associated reduction in diversity is a therapeutic normalisation**, not dysbiosis.

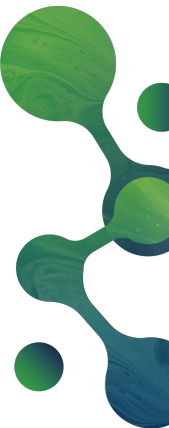
Local (vaginal) oestrogen therapy has the strongest evidence for reversing dysbiosis and improving symptoms such as dryness and dyspareunia.

Systemic HRT also influences the vaginal microbiome, but local application usually achieves quicker and more pronounced microbial restoration.

Combining oestrogen with targeted probiotics (e.g., Lactobacillus crispatus, L. rhamnosus, L. reuteri) may improve outcomes

Lan Y, et al Menopause. 2024 Nov 1;31(11):1014-1023

Spurbeck et al . Future Microbiol. 2011 May;6(5):567-82.



HRT – Gut Microbiome

Altered microbial composition - Women using HRT exhibit **distinct gut microbial profiles** compared with non-users. Differences occur at the **community level**, rather than consistent changes in single taxa.

Increased or preserved microbial diversity - Several human studies report **higher α -diversity** in postmenopausal women on HRT. This suggests HRT may **preserve microbiome resilience** that otherwise declines with oestrogen loss. This may have implications body system wide e.g SCFA production and metabolic health

Premature Ovarian Insufficiency (POI)

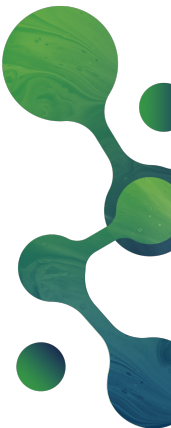
HRT shows **stronger microbiome effects** than in natural menopause

Reduced gut dysbiosis

Improved microbial balance

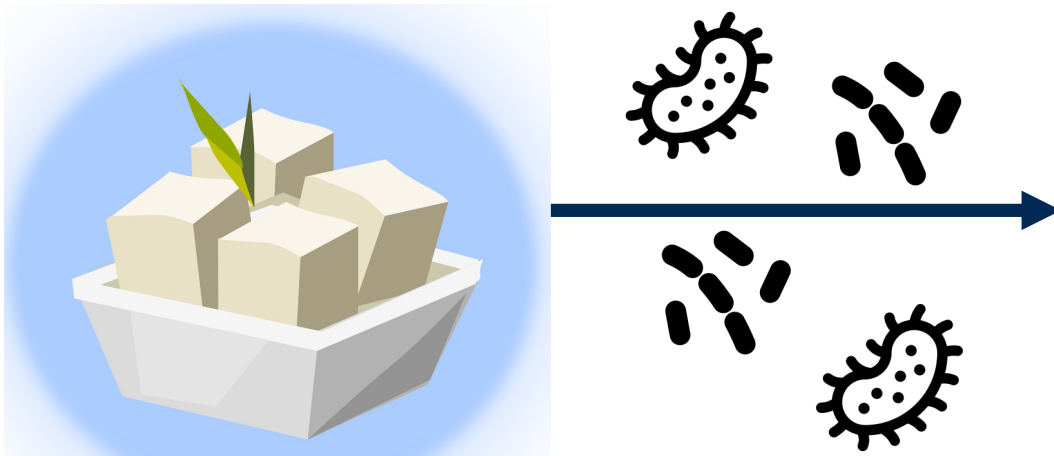
Lower inflammatory, oxidative stress, and fibrotic biomarkers

Supports the concept that **earlier oestrogen loss has more profound gut consequences**, making HRT particularly critical.



Understanding the Microbiome-Phytoestrogen Axis

Research increasingly describes phytoestrogens as "pro-drugs": inactive precursors that require a functional "gut bioreactor" to be unlocked.

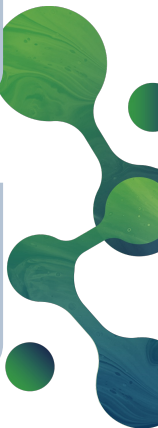


Note: only 25–35% of Western women (and ~50% of Asian women) have the microbial machinery to produce Equol.

Diversity vs. Specificity: Whether isoflavones meaningfully reduce hot flashes depends largely on equol-producer status. Women whose microbiome converts daidzein into S-Equol respond substantially better; non-producers see only modest benefit. Microbial diversity is therefore the key variable.

Different types of phytoestrogen have different benefits, need specific microbes: dietary diversity and microbial diversity important

Multiple Benefits - Urolithin A (from pomegranate) and Enterolactone (from flax) aid hormone support and aid gut barrier support



Phytoestrogens & the Microbiome

Category	Component	Microbial Action	Clinical Role in Menopause	Bacterial Players
The Estrobolome	Endogenous oestrogen	Deconjugation: Uses beta-glucuronidase to "unpack" and recycle remaining oestrogen.	Modulates - Prevents the steep "crash" of your own oestrogen.	Bacteroides: Escherichia coli: Clostridium:
Phytoestrogen Metabolism	Isoflavones (Soy, Red Clover)	Converts Daidzein into Equol (Potent ER beta agonist).	Hot flashes and bone density benefit greatest in equol producers	Adlercreutzia, Eggerthella, Asaccharobacter
Phytoestrogen Metabolism	Lignans (Flax, Sesame)	Converts plant precursors into Enterolactone (ENL) . Conversion requires a "consortium" of bacteria rather than a single species.	Metabolic: Associated with improved lipid profiles /reduced cardiovascular risk markers (largely observational evidence).	Bacteroides, Bifidobacterium, Eubacterium
Phytoestrogen Metabolism	Ellagitannins (Pomegranate, Walnuts)	Converts precursors into Urolithin A .	Muscle Health Improves mitochondrial health, may help prevent Sarcopenia	Gordonibacter, Ellagibacter
Phytoestrogen Metabolism	Coumestans (Sprouts, Clover)	Mostly direct receptor binding with minimal conversion.	Bone Support highest ERβ affinity of dietary phytoestrogens; direct bone-building effects shown in preclinical studies	Minimal microbial processing

Improving microbiome diversity and balance



Dietary diversity
Mediterranean style,
avoidance of additives,
sweeteners etc



Increase fibre from
plants: vegetables, fruits,
seeds, nuts, wholegrains



Functional foods for
motility - psyllium, kiwi
fruit/ flaxseed / prunes



Omega 3 fatty acids &
specific vitamins (e.g
riboflavin)



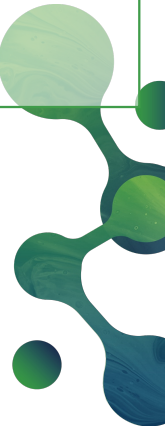
Fermented foods



Probiotic, Fibre and
Prebiotic
Supplementation



Polyphenols

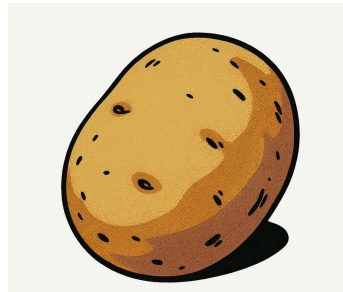


Multiple Roles of Fibre

Fibre isn't just for regularity; it supports microbial health, SCFA production, gut barrier function, is a substrate for beta-glucuronidase-producing bacteria and phytoestrogen-active microbes



Soluble Fibre: Oats, Beans, and Legumes. These help regulate transit time, supports blood glucose, lipid health and allows bacteria like *Adlercreutzia* more time to ferment isoflavones into Equol.



Resistant Starch: Cooked and cooled potatoes/rice and green bananas. Resistant starch increases *Ruminococcus* and *Faecalibacterium prausnitzii*. Bifidobacterium species, supporting SCFA production, improving insulin sensitivity and lipid metabolism



Inulin-Rich Foods: Garlic, Onions, Asparagus, and Artichokes. These prebiotics selectively feed estrobolome-associated bacteria, promoting the beta-glucuronidase activity essential for recycling oestrogen and maintaining hormonal balance



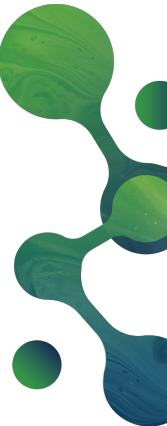
Plant Focused Diets

Switching to a plant-heavy diet (especially those rich in phytoestrogens) may have additional benefits via the gut microbiome at menopause

One RCT found a low-fat, vegan diet including cooked soybeans (½ cup [86g]/day) for 12 weeks reduced moderate-to-severe hot flashes by 88%, with 59% of women becoming completely free of moderate-to-severe hot flashes

Changes in *Porphyromonas* and *Prevotella corporis* correlated with hot flashes; changes in *Clostridium asparagiforme* correlated with changes in severe hot flashes.

Lower fat, high fibre diets: High saturated fat can decrease *Akkermansia*, whereas plant-based fibres increase it.



Prebiotic Fibres at Menopause

Selective feeding of estrobolome-associated bacteria to support oestrogen recycling

Butyrate production to maintain gut barrier integrity and reduce endotoxin load

Microbial diversity — which declines at menopause and is associated with insulin resistance and cardiometabolic risk

Prebiotic fibres support *Akkermansia muciniphila* abundance - enhancing mucin layer integrity and metabolic health

Examples of Prebiotic Fibres

Fructans (Inulin, FOS): Chicory root, onions, garlic, leeks

β -Glucans: Oats, barley, mushrooms

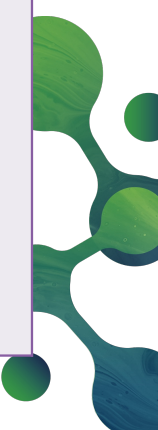
Galactomannans (incl. PHGG): Legumes, guar gum

Arabinogalactans / Arabinoxylans: Apples, pears, berries, whole grains

Xylooligosaccharides (XOS): Corn cobs, bamboo shoots

PHGG (Partially Hydrolysed Guar Gum):

A low-gas, well-tolerated galactomannan prebiotic with strong evidence in gut barrier support and functional gut symptoms.



PHGG (Partially Hydrolysed Guar Gum) *Prebiotic fibre*



Improves transit time, eases constipation, bloating, pain



Supports Immune function

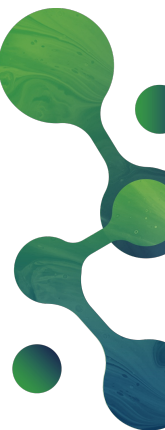


Supplementation with a combination of probiotics, PHGG, and polyphenol-rich extracts significantly improved the quality of life in IBS patients via modulation of immune markers, increased beneficial SCFAs Wierzbicka et al 2025

production



Practical Advantage: Low-FODMAP and non-viscous; better tolerated than inulin for IBS. 5g daily. Addition of *Lactiplantibacillus plantarum* (Lpla33™) as in Ultraflora Fibre may improve motility and reduce abdominal bloating.



Polyphenols

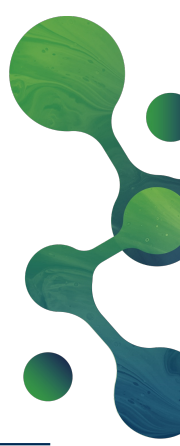
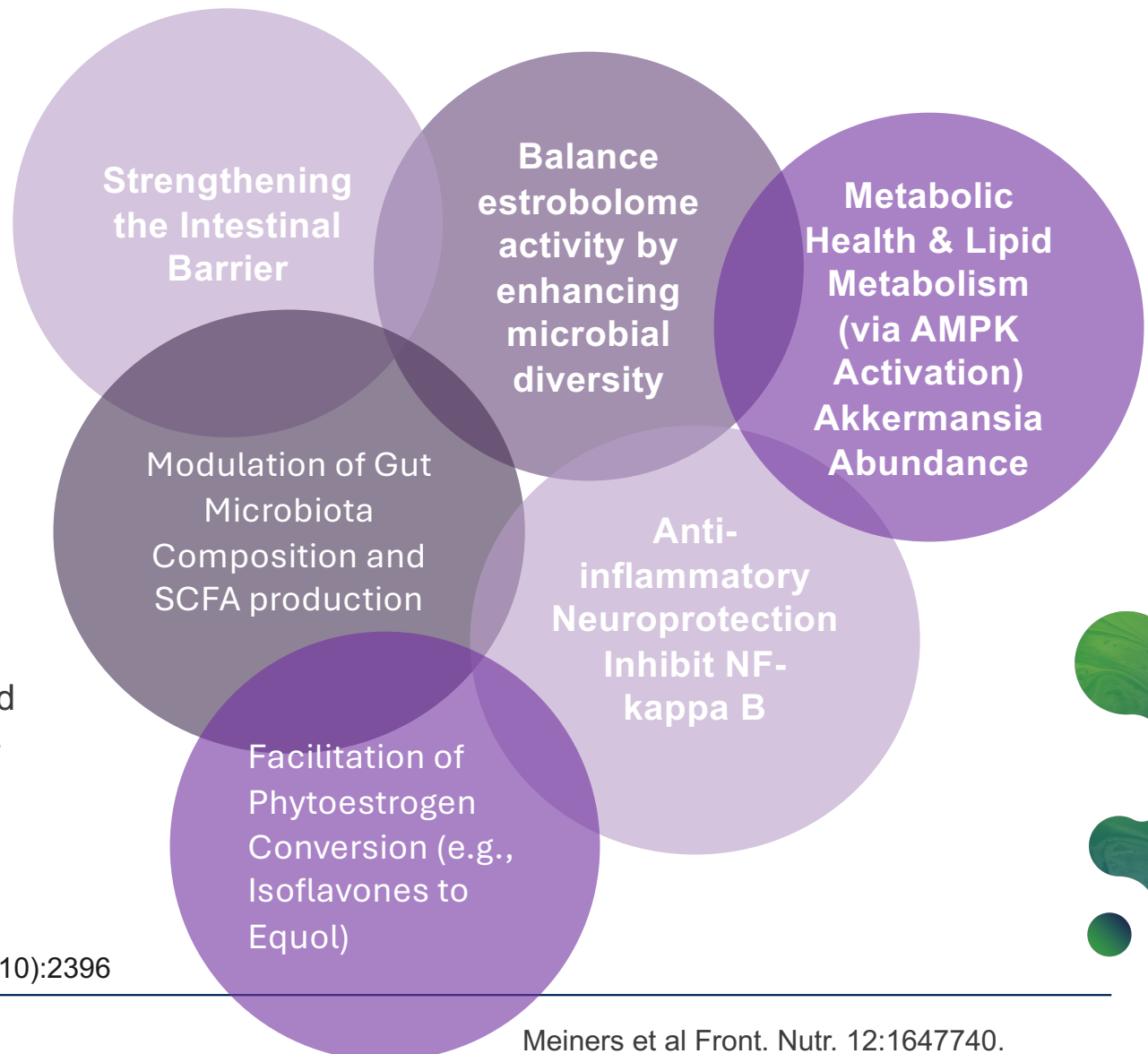


Only 5–10% of polyphenols are absorbed in the small intestine. The remaining 90–95% reach the colon - transformed by microbes into active phenolic acids and stimulate SCFA production.

Wilder-Smith et al *Nutrients*. 2023 May 20;15(10):2396



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Meiners et al *Front. Nutr.* 12:1647740.
Rudrapal M, et al . 2026 *Front. Pharmacol.* 16:1710088.

Use of Probiotics – protective role at Menopause



Inhibit visceral hypersensitivity
Improve intestinal motor function

Metabolic Health

Inhibit pathogenic bacteria

Gut-Brain Health

Strengthen barrier function

Vaginal Health

Regulate GI pH

Gut-Bone Axis

Regulate immunity /
inflammation

Modulate the Estrobolome e.g L.
brevis KABP052

Zhang J, et al. Medicine (Baltimore). 2020 Feb;99(7):e19107. doi: 10.1097/MD.00000000000019107

Use of Multi- strain formulas



Prediabetes + metabolic syndrome

Multi-strain Lactobacillus + Bifidobacterium blend

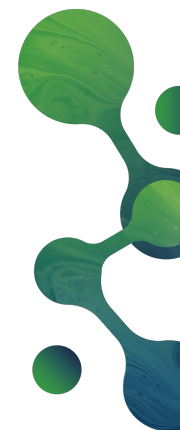
Intervention: 6g/day multi-species probiotic - 2 billion Group with FOS added
12 & 24 weeks

Mechanisms Suggested

- Improved gut barrier function
- Reduced endotoxemia
- Modulation of gut microbiota composition
- Reduced systemic inflammation
- Improved short-chain fatty acid production

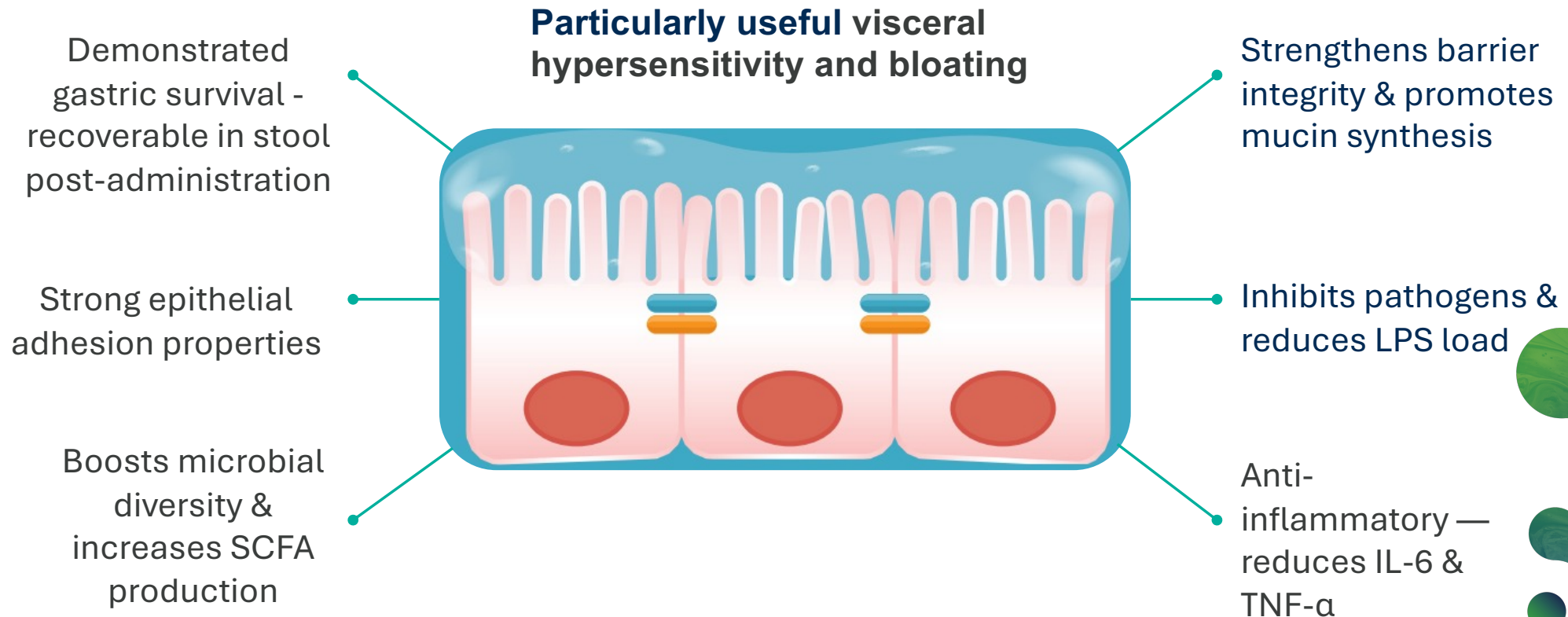
Key Outcomes (12 Weeks)

↓ Fasting glucose and improved HOMA-IR (greater effect with synbiotic)
↓ Triglycerides, ↑ HDL (modest total cholesterol change)
↓ Inflammatory markers (CRP trend)
Some participants no longer met metabolic syndrome criteria



L. acidophilus NCFM® & B. lactis Bi-07®

A well-researched strain combination with targeted mechanisms to support gut health and symptoms



Ringel-Kulka et al. J Clin Gastroenterol. 2011 Jul;45(6):518-25

Rousseaux et al. Nature Medicine February 2007 13(1):35-7 DOI:10.1038/nm1521
Ringel - Kulka et al Aliment Pharmacol Ther. 2014 Jul;40(2):200-7

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Summary: Supporting the Menopausal Microbiome

Hormonal Impact: Menopause shifts the gut toward a pro-inflammatory state, directly increasing metabolic, bone, and cardiovascular risks.

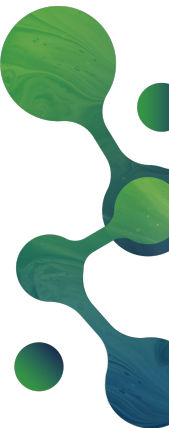
Restore Microbial Diversity: Aim to increase diversity to counter the low-diversity, pro-inflammatory "M-type" profile seen in menopause - fibres, PHGG, high polyphenol intake (also helps reduce LPS metabolic endotoxemia and barrier health)

Support the Estrobolome: Use targeted fibres and probiotics to optimise oestrogen recycling and the conversion of isoflavones into Equol and Urolithin A.

Targeted Supplementation: Gut and Barrier: *L. acidophilus* NCFM & *B. lactis* Bi-07.

Vaginal Health: *L. rhamnosus* GR-1 & *L. reuteri* RC-14; **Prebiotic:** PHGG fibre to improve digestive symptoms, motility, and SCFA production.

Integrative Approach: Combine microbiome-focused nutrition with stress management and sleep hygiene to mitigate the systemic impact of hormonal decline.



Key Products From Metagenics

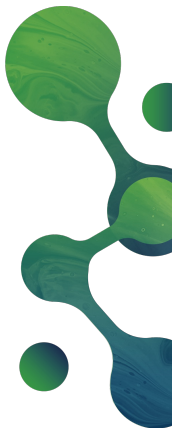
- Ultraflora Fibre (PHGG)
- Ultraflora Complete for Women
- Ultraflora Complete
- Ultraflora Restore
- OmegaGenics High Strength
- Multi Essentials for Women 50+ Multivitamin

Recipes

1. Vanilla Berry Chia Pots
2. Cinnamon Spiced Granola
3. Smashed Edamame Beans with lemon and capers
4. Chunky Minestrone Soup
5. Sicilian Chickpea Quinoa Bowl
6. Roasted Vegetables, Puy Lentils and Harissa Dressing
7. Red rice salad with pomegranate, feta with pistachios
8. Thai Green Chicken Curry
9. Tempeh and Mushroom Bolognese
10. Banana Chocolate Chip Bread



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Cardiometabolic Health and Menopause Protocol

This protocol provides a comprehensive, evidence-informed approach to understanding and managing the profound cardiometabolic changes that emerge during the perimenopausal and menopausal transition.



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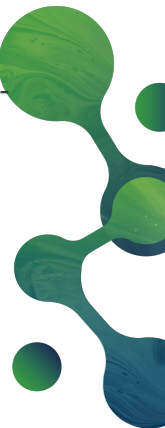
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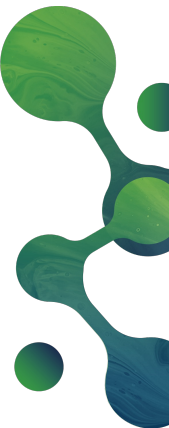
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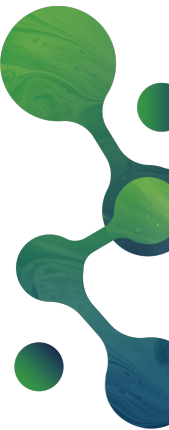
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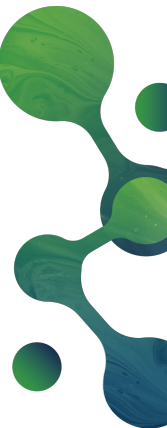
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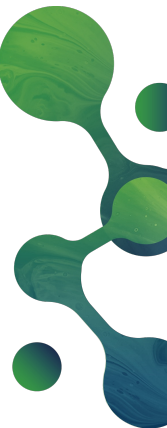
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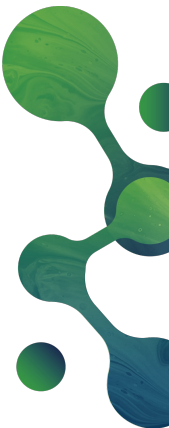
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