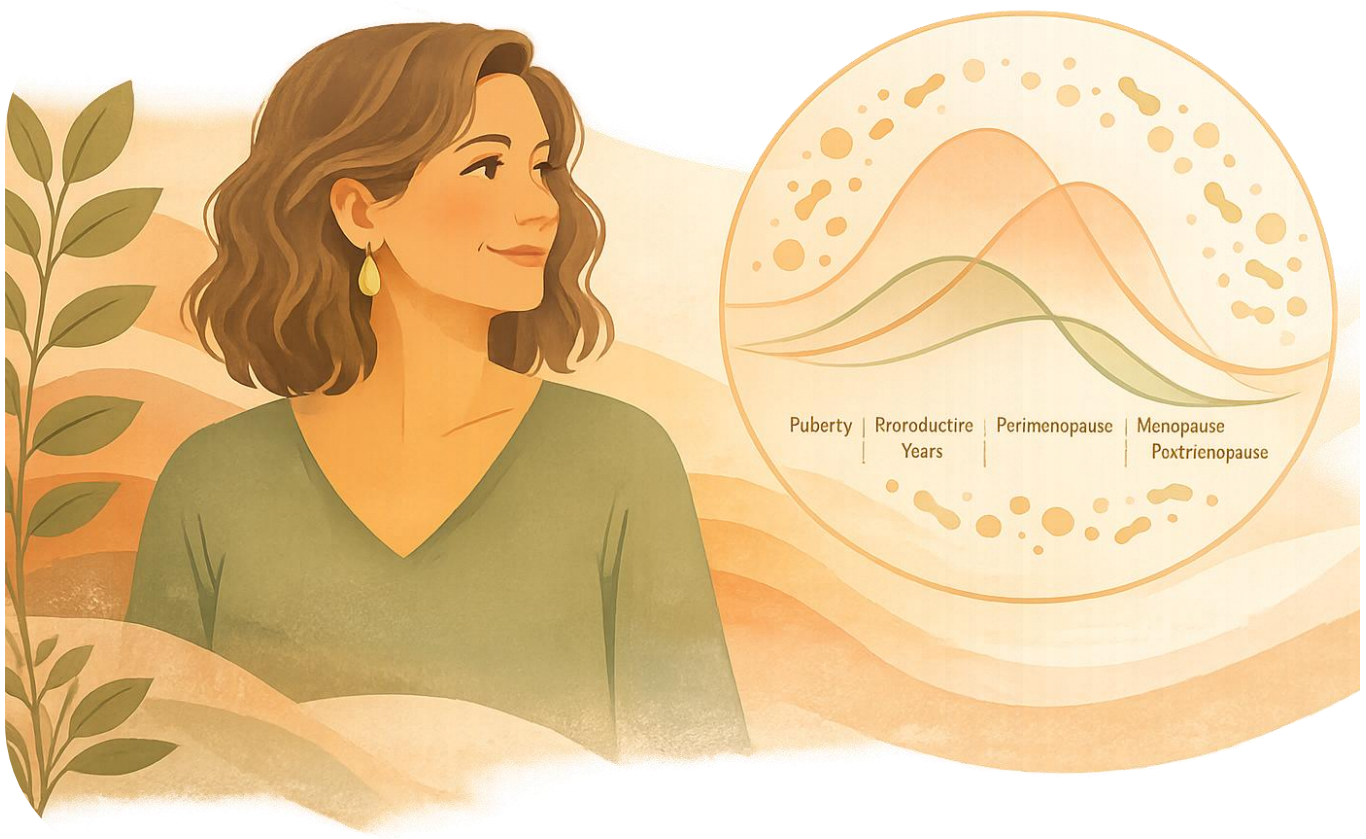
Microbiome Center

The role of microbiome during menopause

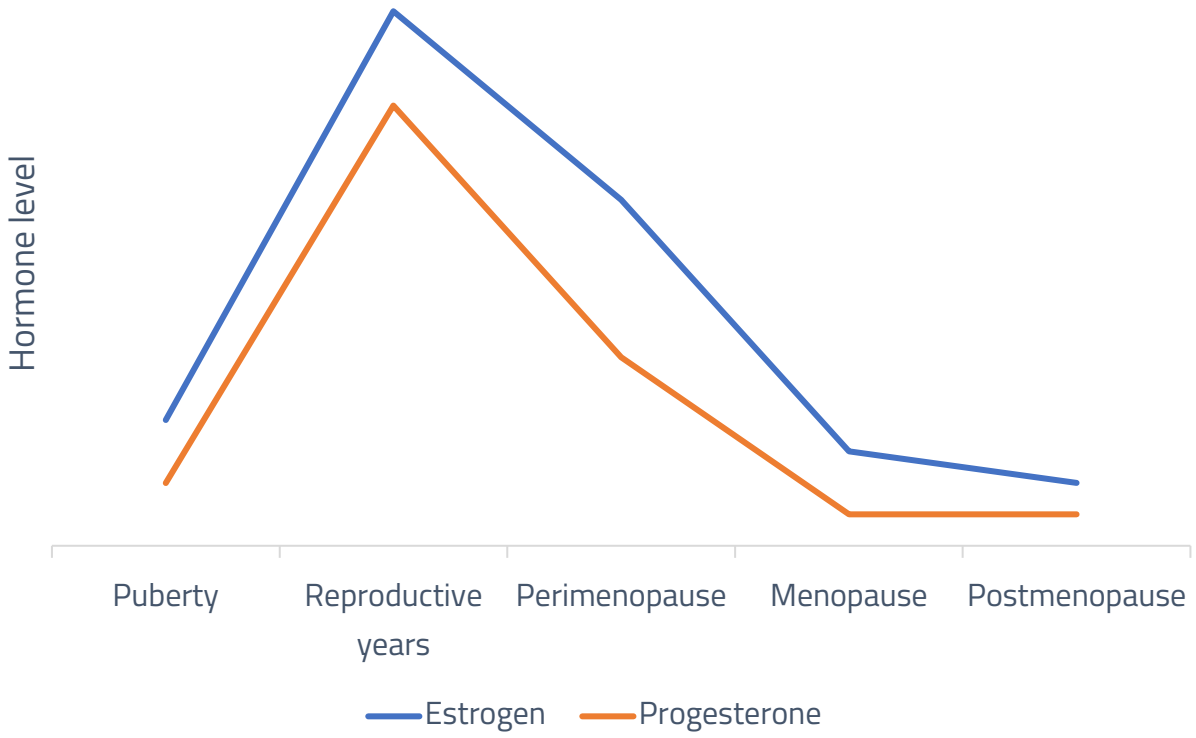
Dr. Mariya Petrova



Women’s hormonal journey

Hormonal changes across a woman's life

Estrogen and progesterone shift from activation to persistently low levels.



KEY TREND INSIGHTS

01 Puberty: hormones; reproductive cycles

02 Perimenopause: irregular estrogen, early progesterone decline

03 Menopause brings a marked estrogen drop; postmenopause remains persistently low.

1. Patel et al 2025 J Midlife Health . doi: 10.4103/jmh.jmh_75_25
2. Zacur et al 2006 Headache doi: 10.1111/j.1526-4610.2006.00554.x.

Understanding menopause

01

PERIMENOPAUSE

The transition leading to menopause. Begins in the early-to-mid 40s
Can last 5-10 years

02

MENOPAUSE

The stage is reached after 12 consecutive months without menstruation
Menopause is a single moment in time

03

POSTMENOPAUSE

Start immediately after the menopause.
Continues for the rest of life

Understanding menopause

01

PERIMENOPAUSE

- Fluctuating estrogen;
- Declining progesterone
- Mostly regular cycles;
- Symptoms: hot flashes; night sweets; mood changes , sleep disturbances; vaginal dryness

02

MENOPAUSE

- Marked decline in estrogen;
- Ovarian activity has essentially ceased
- Once diagnosed, the transition to the postmenopausal begins immediately

03

POSTMENOPAUSE

- Chronically low estrogen;
- Early postmenopause - hot flashes, sleep issues, vaginal dryness, mood changes, nigh sweets
- Late postmenopause – osteoporosis, metabolic and cardiovascular disease, urogenital atrophy

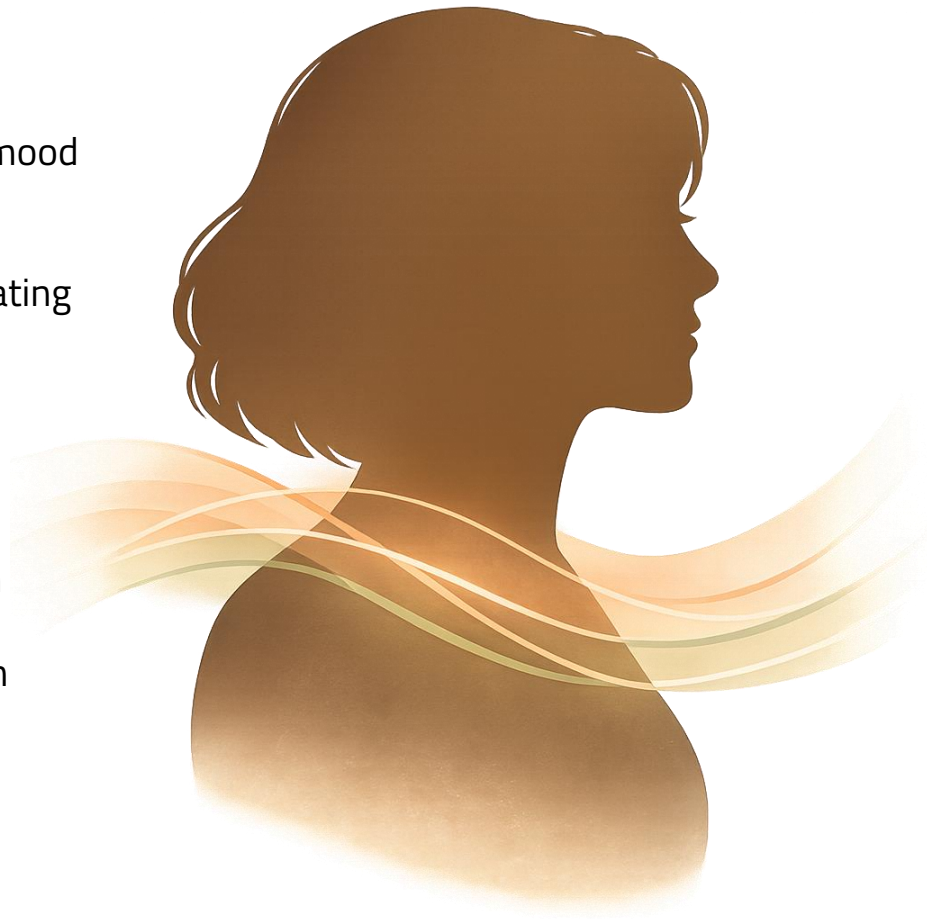
Menopause – how does it feel?

Hot Flashes

Mind and Mood
- Mood swings low mood
- Anxious feelings
- Irritability
- Difficulty concentrating
- Brain fog
- Memory issues
- Headaches

Muscles and Joint Pain
- Joint pains/stiffness
- Long-term back pain
- Muscle pain

Energy and Sleep
- Physical exhaustion
- Mental exhaustion
- Trouble sleeping



Bone health

Weight changes

Hair, Skin and Nails
- Thinning hair
- Weak or brittle nails
- Itchy and dry skin
- Facial wrinkles
- Loss of skin firmness
- Dark spots

Digestion
- Bloating
- Heartburn
- Upset stomach
- Constipation
- Diarrhea
- Bladder issues

Intimacy
- Low sex dive
- Vaginal dryness
- Painful sex

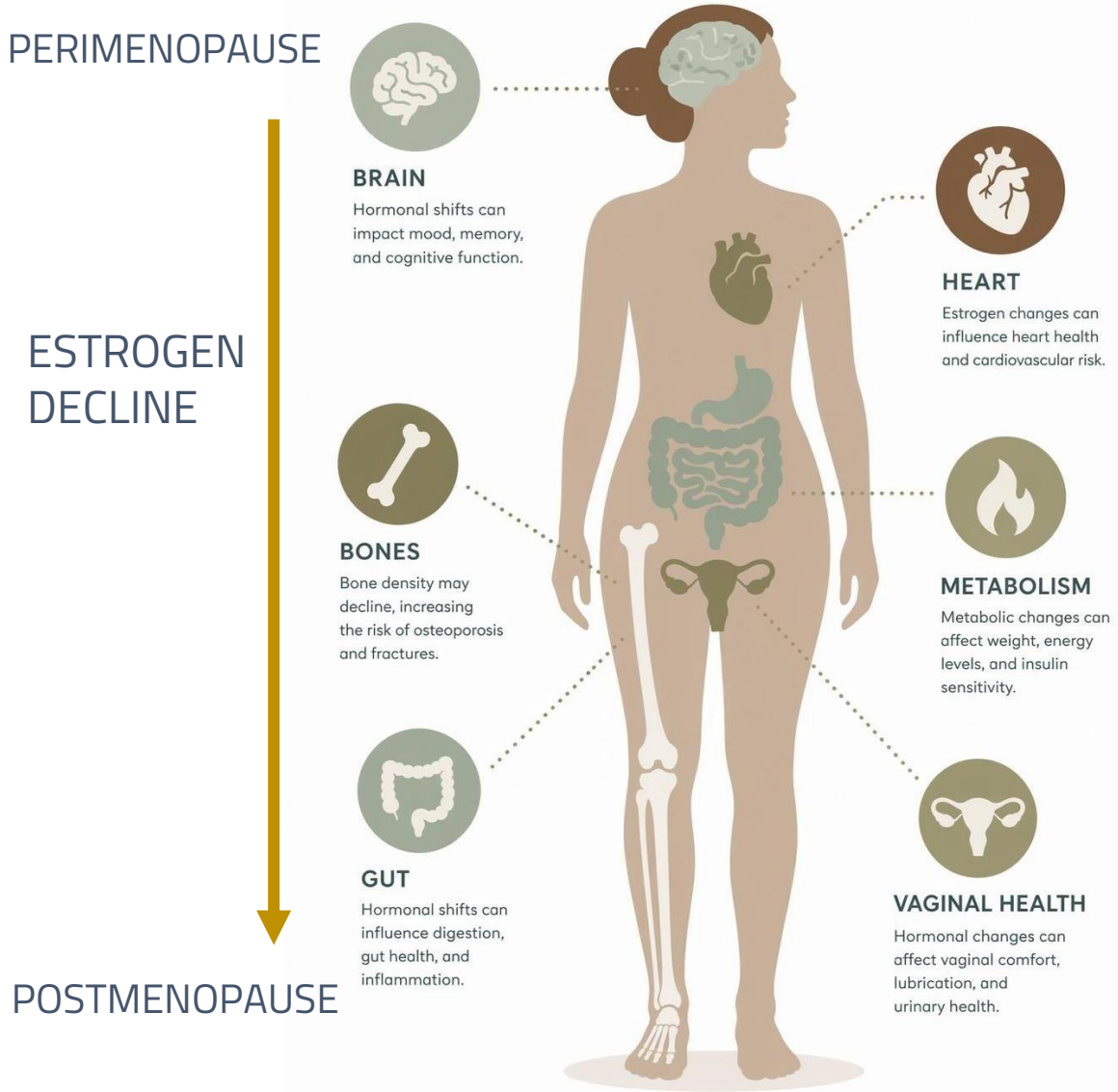
Hormonal Shifts drive Symptoms and Disease risk

01 **Insulin Resistance & Type 2 Diabetes**
Estrogen supports insulin sensitivity and glucose handling
Decline leads to ↑ visceral fat & impaired glucose metabolism
Outcome: Increased risk of metabolic syndrome and T2D

02 **Cardiovascular Disease**
Estrogen protects vascular function and lipid balance
Decline leads to ↑ LDL, ↓ HDL, ↑ vascular stiffness
Outcome: sharply increased CVD risk after menopause

03 **Depression & Cognitive Changes**
Estrogen influences serotonin, dopamine, and brain plasticity
Outcome: mood instability (peri) and ↑ risk of depression and cognitive decline (post)

04 **Thyroid Health**
Estrogen affects thyroid hormone binding and
Outcome: fatigue, weight gain, increased clinical relevance of thyroid disorders



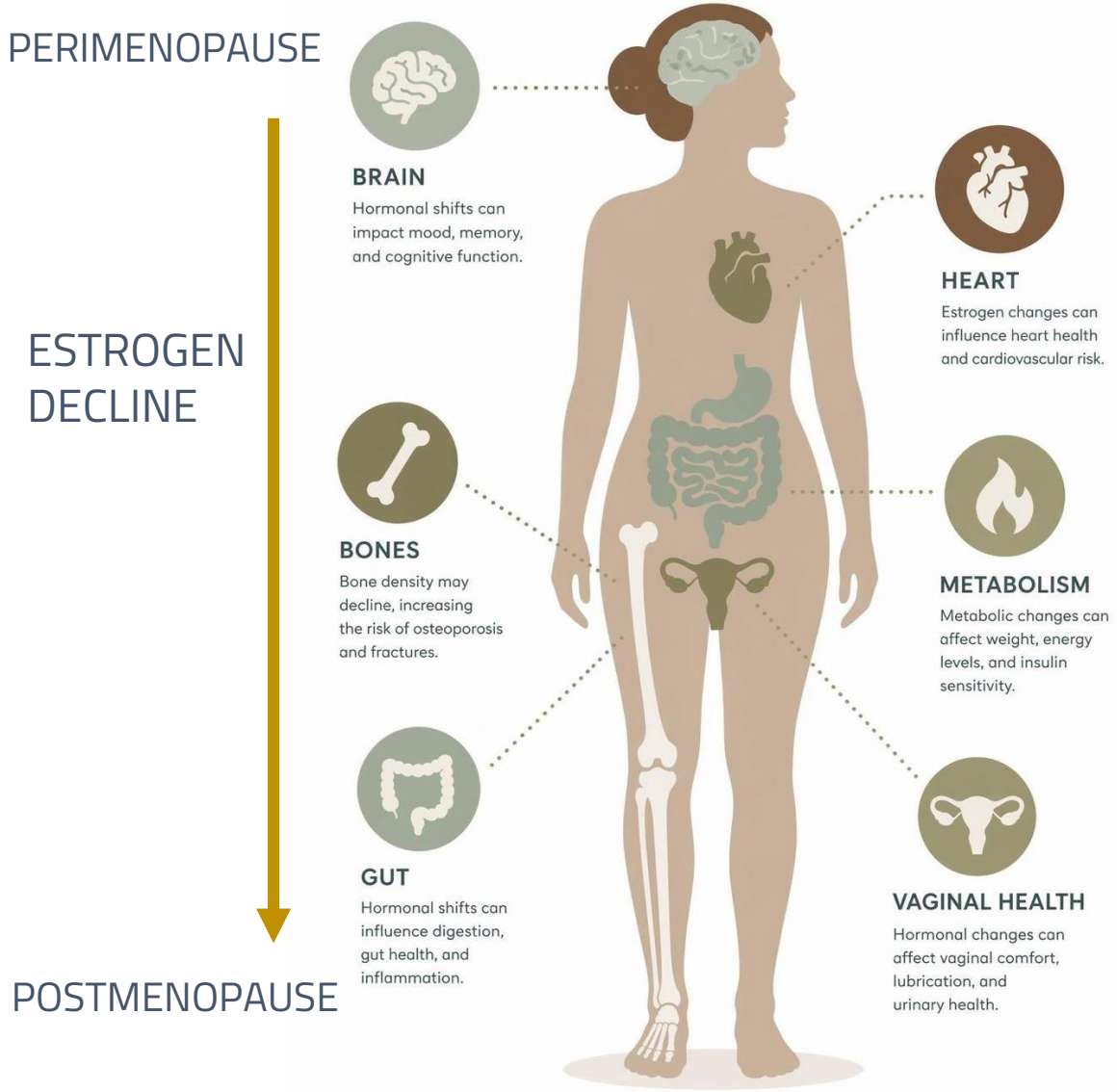
1. Lim et al 2026 Nutrients https://doi.org/10.3390/nu18071052
2. Cuozzo et al 2026 PNS DOI: https://doi.org/10.1017/S0029665126102201
3. Wang et al. 2025 Frontiers in Enddocrinology https://doi.org/10.3389/fendo.2025.1562332

Hormonal Shifts drive Symptoms and Disease risk

05 **Bone Health**
Estrogen is critical for bone remodeling balance
Decline leads to ↑ osteoclast activity (bone breakdown)
Outcome: accelerated bone loss increased risk of osteopenia and osteoporosishigher fracture risk

06 **Vaginal Health**
Estrogen maintains vaginal epithelium thickness glycogen → Lactobacillus growth and low pH
Decline leads to ↓ glycogen ↓ Lactobacillus↑ pH
Outcome: vaginal dryness, irritation, infections, Genitourinary Syndrome of Menopause (GSM)

07 **Gut Health**
Estrogen and gut microbiota are tightly linked (estrobolome)
Menopause leads to altered gut microbiome composition leading to ↑ low-grade inflammation
Outcome: contributes to metabolic dysfunction, systemic inflammation, hormone imbalance



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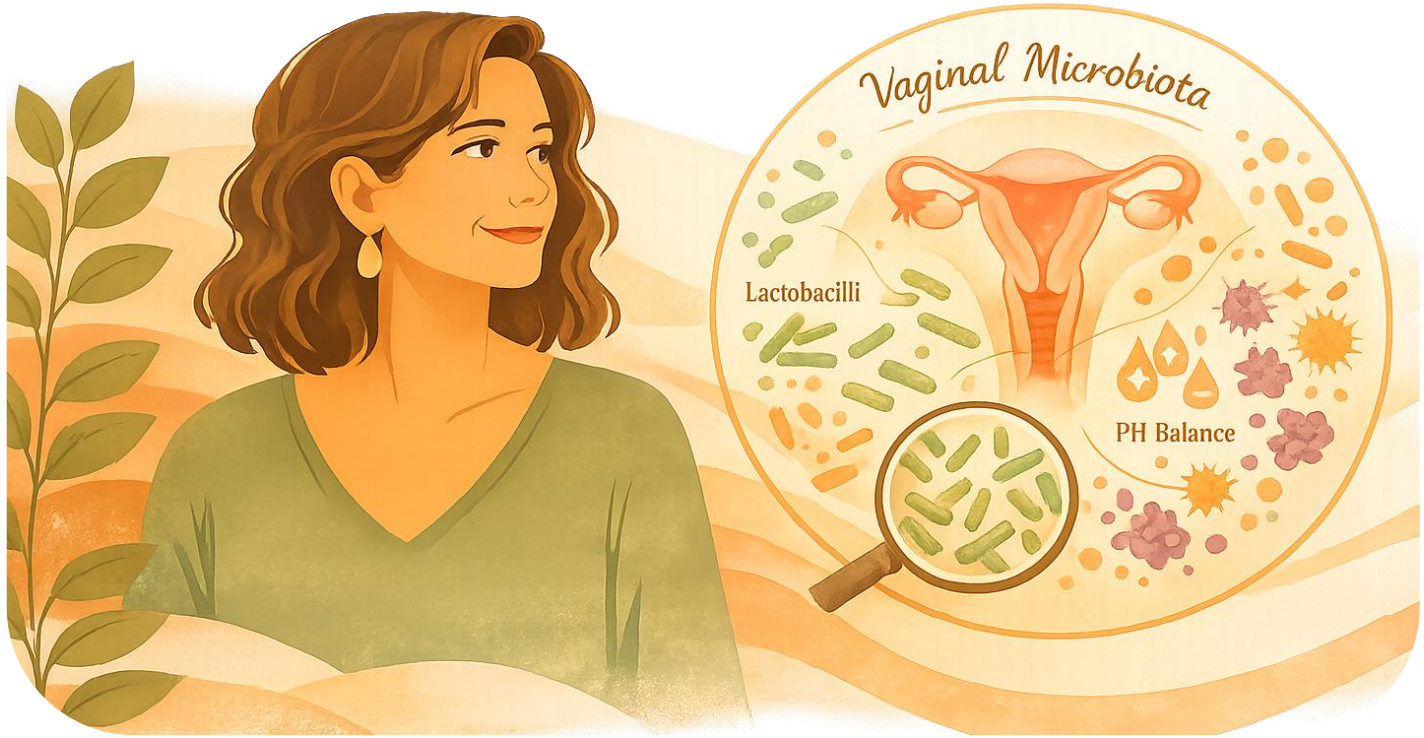
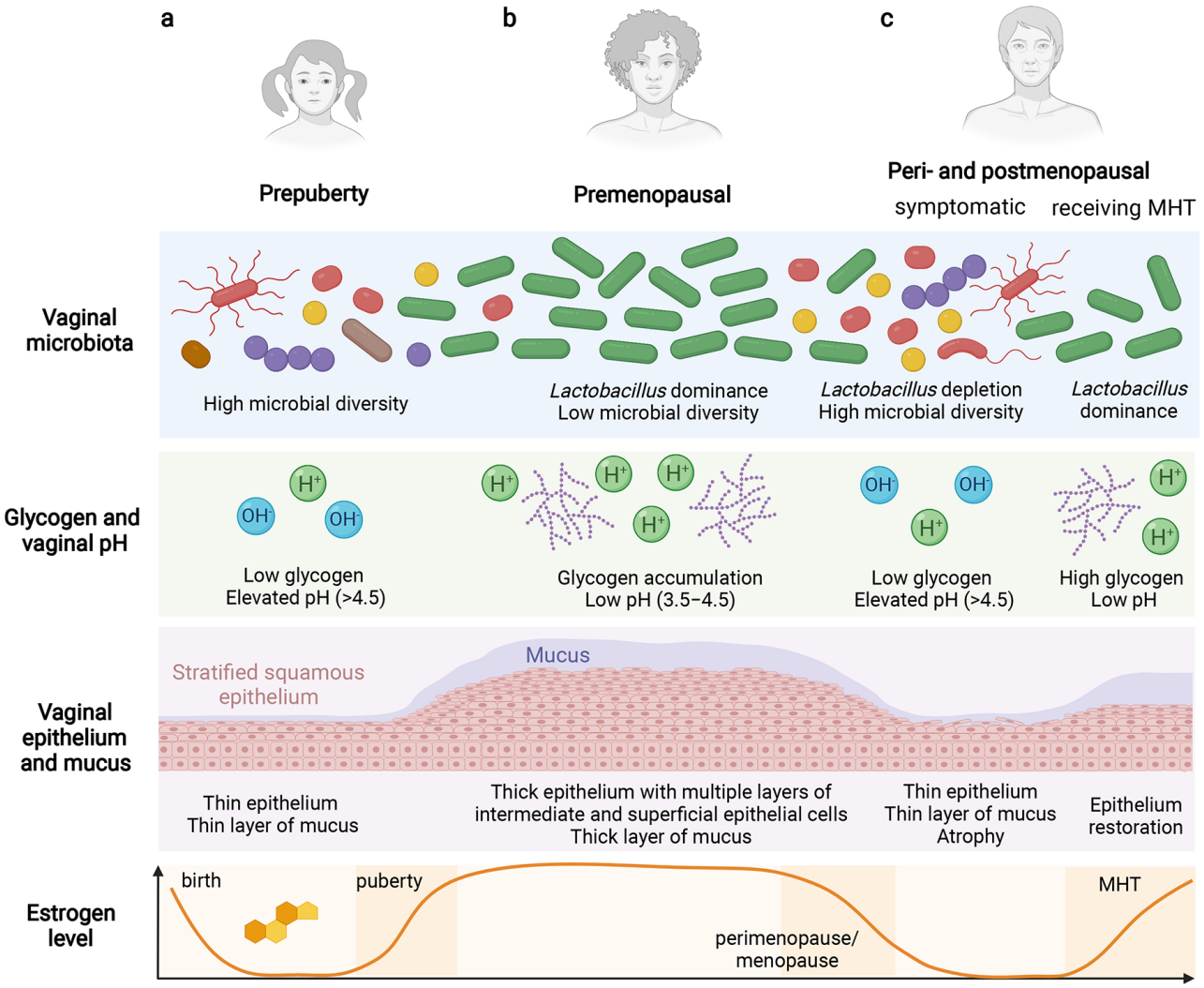


Vaginal microbiota during menopause

Vaginal microbiome across a woman's life[1]

- Before puberty: High microbial diversity, neutral pH, low estrogen.
- Reproductive age: Estrogen supports Lactobacillus dominance and low vaginal pH.
- Menopause: Reduced estrogen decreases Lactobacillus, increases pH and microbial diversity.
- Clinical relevance: Associated with vaginal atrophy and genitourinary symptoms; vaginal estrogen may help restore microbiome balance.



1. Laniewski et al 2022 Nat Microbiol doi: 10.1038/s41564-022-01071-6

Optimal vaginal microbiome during reproductive age

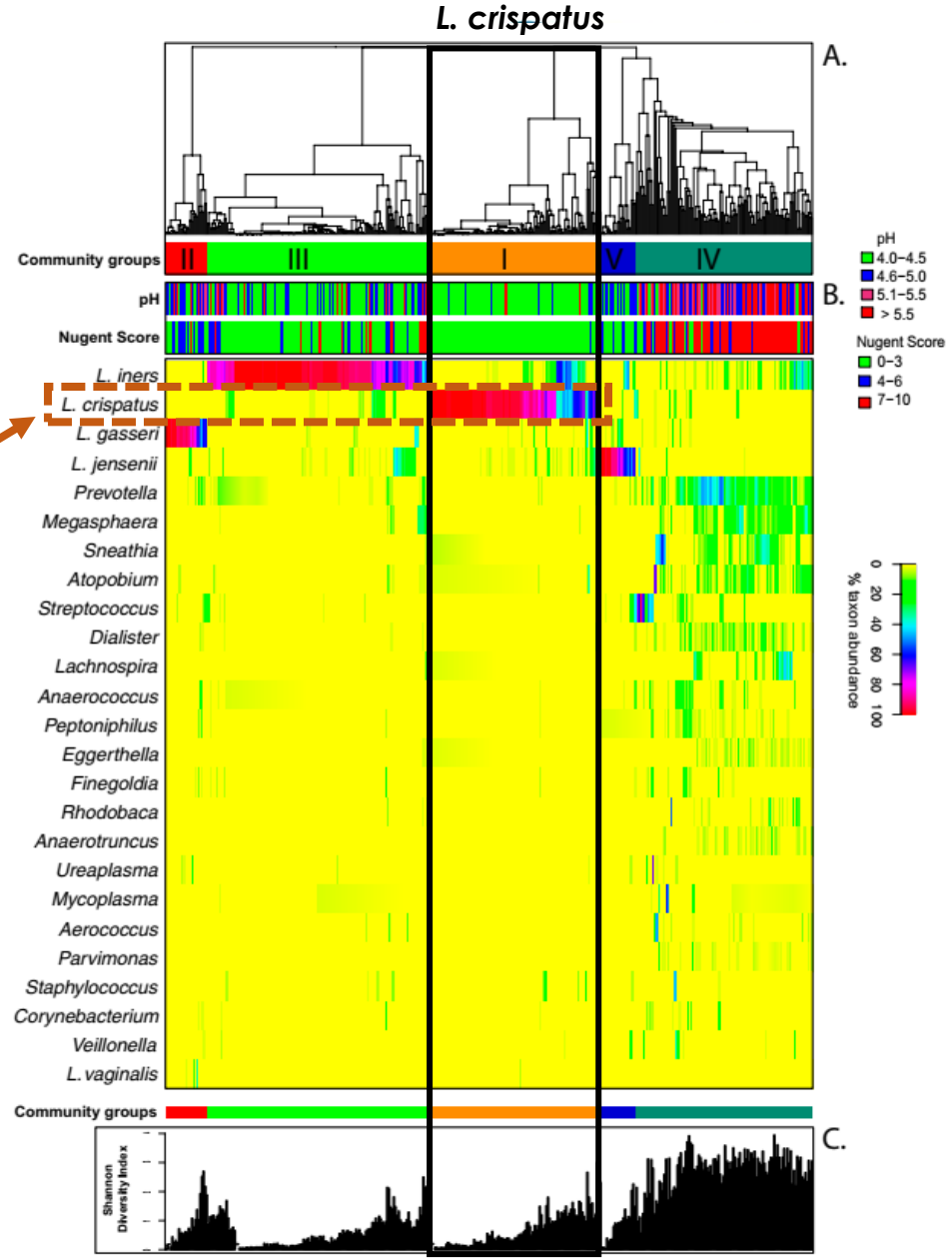
Optimal vaginal microbiota is:

- characterized with low diversity
- dominated by *Lactobacillus* species
- low pH between 3.8 -4.5

Community State Types[1].

- CST 1 – ***L. crispatus* dominated; most associated with health**
- CST 2 – *L. gasseri* dominated
- CST 3 – *L. inres* dominated; benefits under question
- CST 4 – high diversity, non-*Lactobacillus* dominated [2,3]
- CST 5 – *L. jensenii* dominated

Research has built ups since 2011 now each of the CST has been divided into subcategories



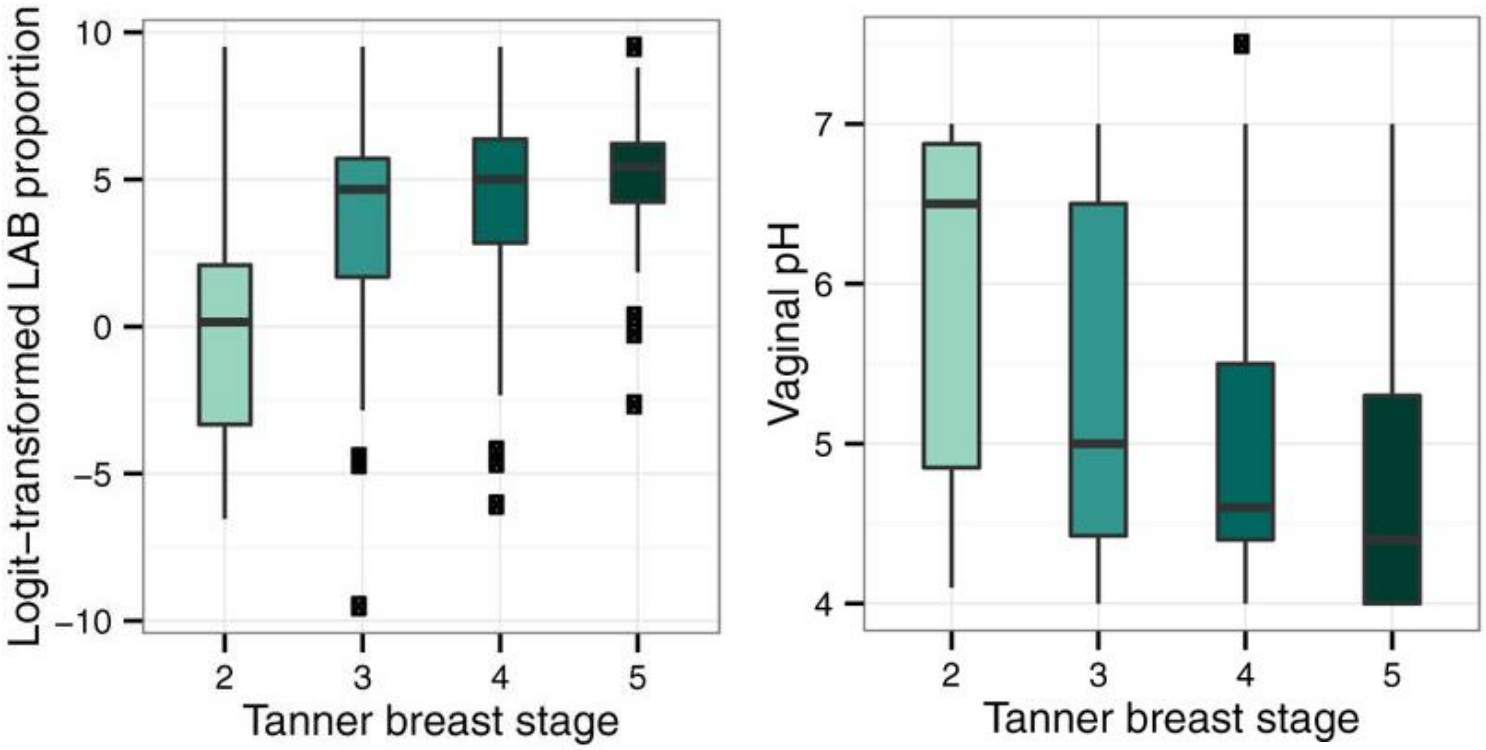
1. Ravel, J. et al. Proc Natl Acad Sci U S A 108, 4680–4687 (2011)
2. Verstraelen, H. et al. Journal of Lower Genital Tract Disease 26, 73 (2022)
3. Gajer, P. et al. Sci Transl Med 4, 132ra52 (2012)

Vaginal microbiome: prepuberty/premenarche

Longitudinal research shows transition of vaginal microbiome from premenarche (~11y/o) to post-menarche[1].

BV-like microbiome gradually shifts toward an adult-like Lactobacillus-dominated microbiome[1]:

- In almost all girls the microbiome changed to *Lactobacillus*-dominant after menache. In some girls already at baseline.
- Transition occurred before or shortly after menarche
- Various trajectories occur, e.g. *L. iners*-dominated to *L. crispatus*-dominated.



1. Hickey, R. J. et al. mBio (2015)

Vaginal microbiome: postmenopausal

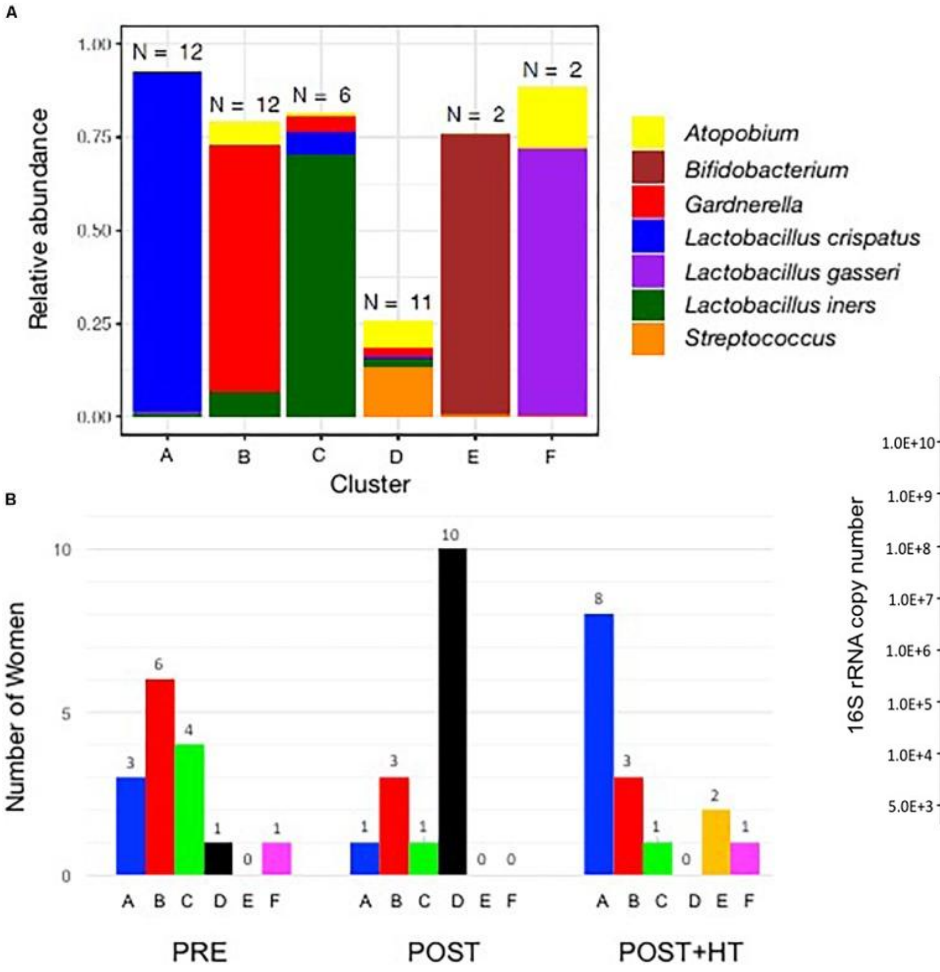
Estrogen levels strongly affect the vaginal microbiota[1,2,3].

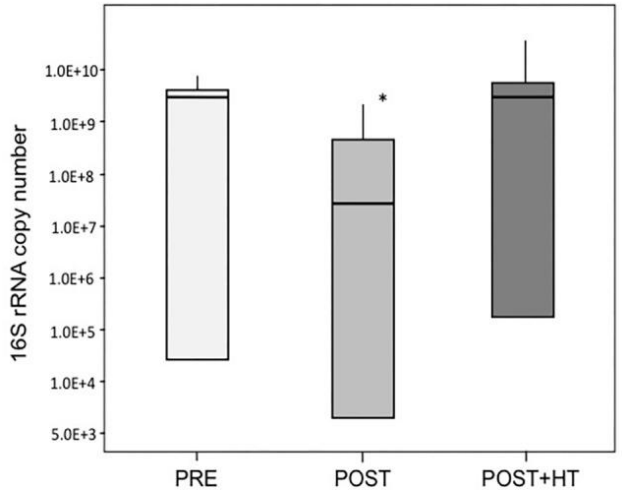
Differences between[1,3]

- Premenopausal
- Postmenopausal
- Postmenopausal with hormone replacement therapy

Postmenopausal women had:

- Much more diverse microbiome without a single dominant species and few lactobacilli
- High prevalence of CST-IV
- 10x lower total abundance

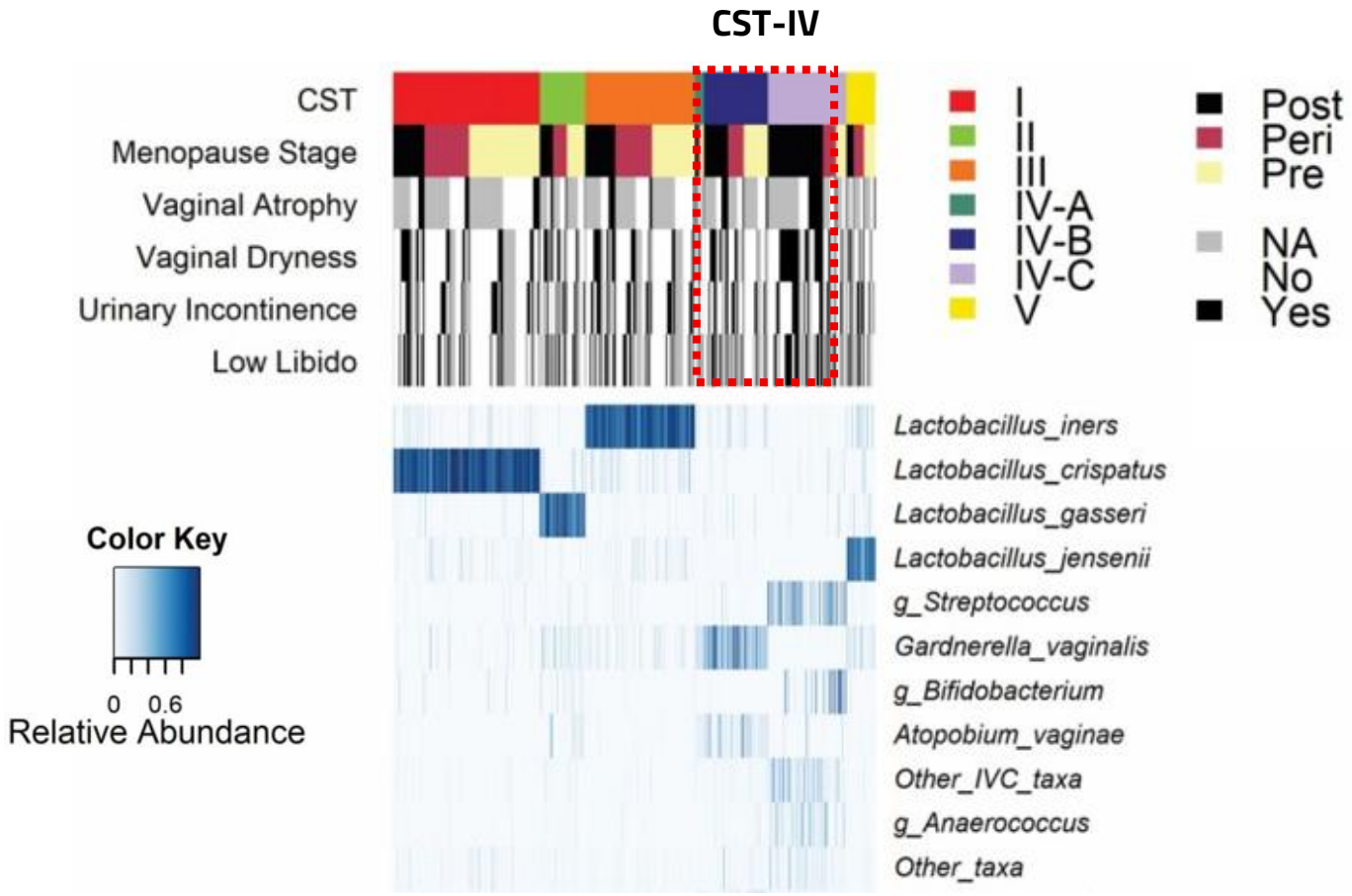




1. Gliniewicz, K. et al. Frontiers in Microbiology 10, (2019)
2. Verstraelen, H. et al. Journal of Lower Genital Tract Disease 26, 73 (2022)
3. Chen et al Microorganisms (2025)

Association of Vaginal Microbiota With Genitourinary Syndrome of Menopause[1,2]

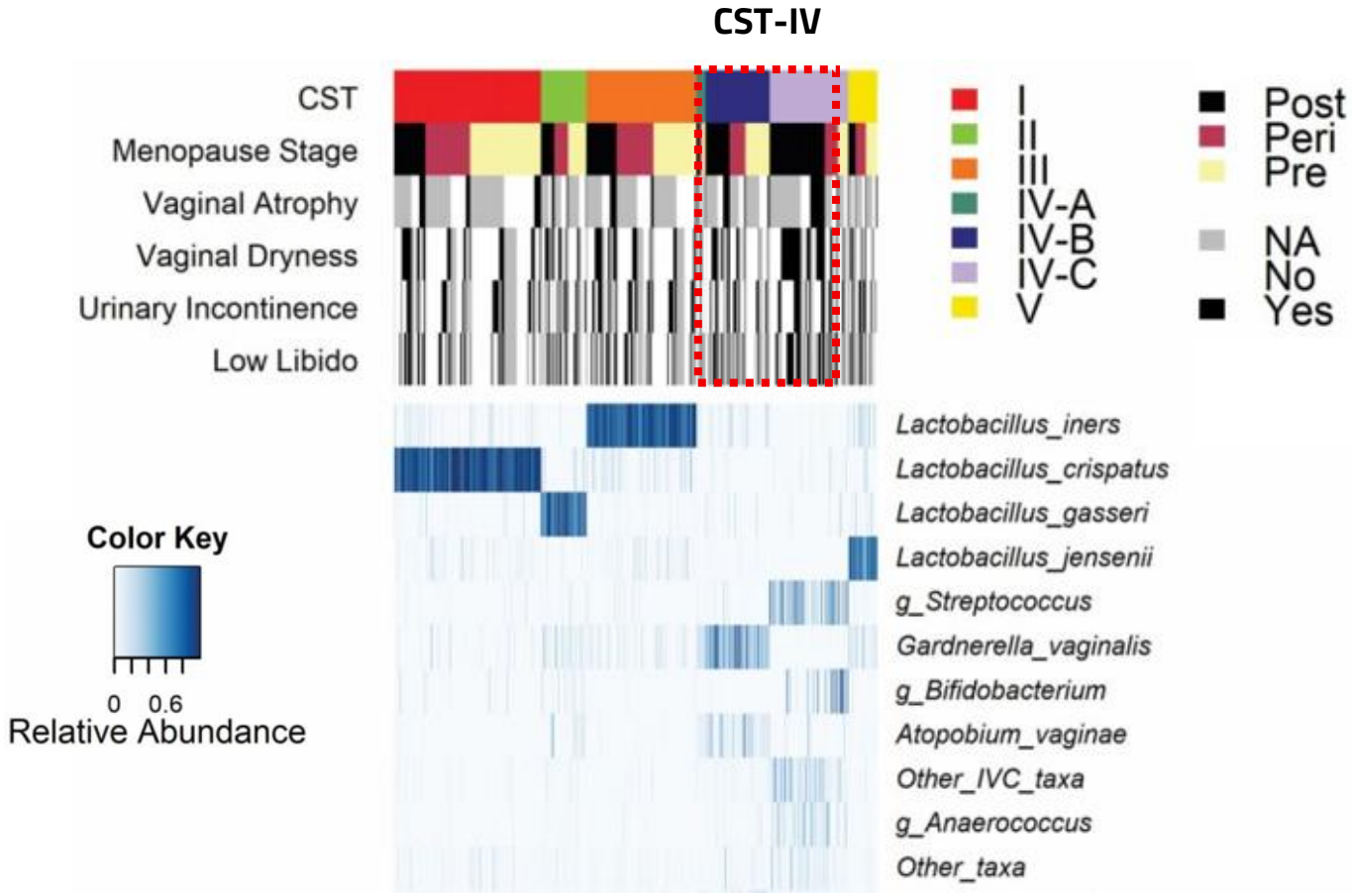
- Low-*Lactobacillus* communities (CST-IV) nearly doubled after menopause
- Strong association between estrogen deficiency and CST-IV states
- Women with *Lactobacillus*-dominated CSTs associated with lower odds of vaginal atrophy and GSM symptoms compared to women with CST-IV.
- *L. crispatus* (CST-I) ~75% lower odds of vaginal atrophy
- The women with the worst vaginal dryness scores were those with CST-IV communities.



1. Shardell et al 2021 J. Gerontol A Biol Sci Med Sci. doi: 10.1093/gerona/glab120
2. Waetjes et al 2023 Menopause doi: 10.1097/GME.0000000000002263

Association of Vaginal Microbiota With Genitourinary Syndrome of Menopause[1,2]

- Postmenopauze women dominate by CST-IV reported the lowest libido. Women with microbiota dominated by *L. gasseri* and *L. jensenii* had the lowest odds of low libido.
- Vaginal dryness and low libido were strongly associated statistically
- Postmenopausal women whose microbiota stayed consistently *Lactobacillus*-dominated across visits had a lower odds of urinary incontinence
- Low-Lactobacillus CST-IV were associated with vaginal dryness, irritation, burning, dyspareunia and vaginal atrophy markers



1. Shardell et al 2021 J. Gerontol A Biol Sci Med Sci. doi: 10.1093/gerona/glab120
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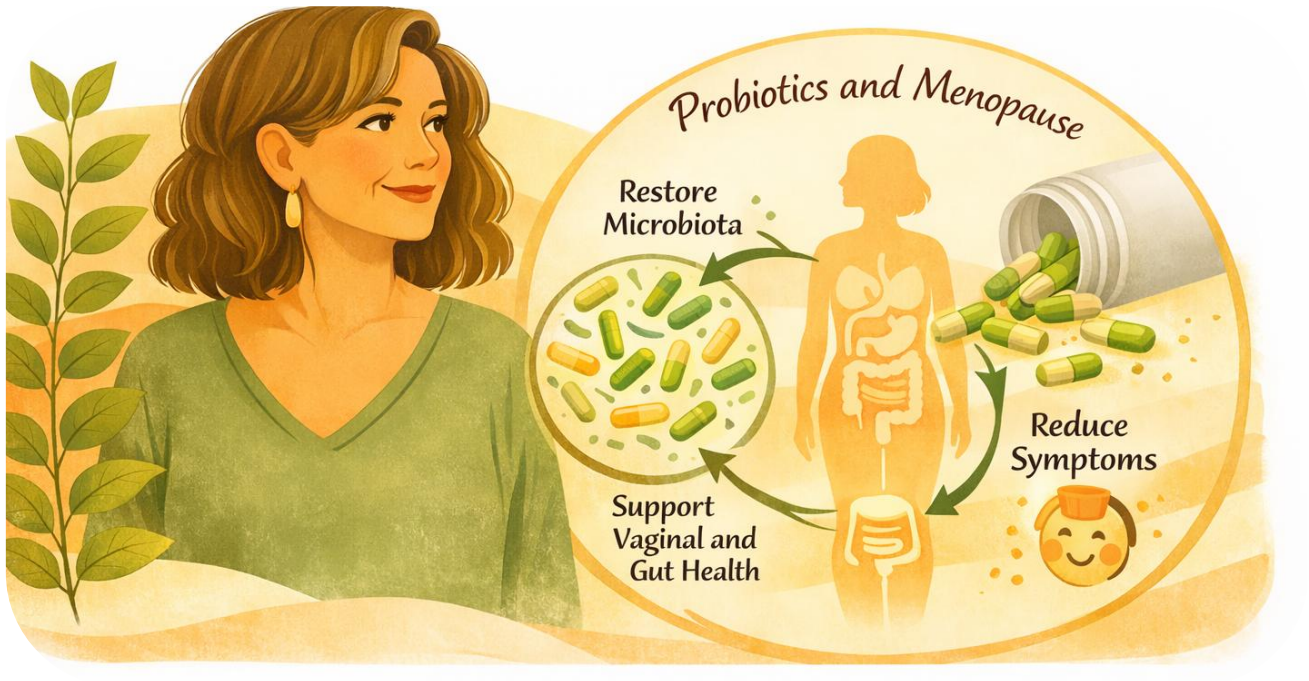
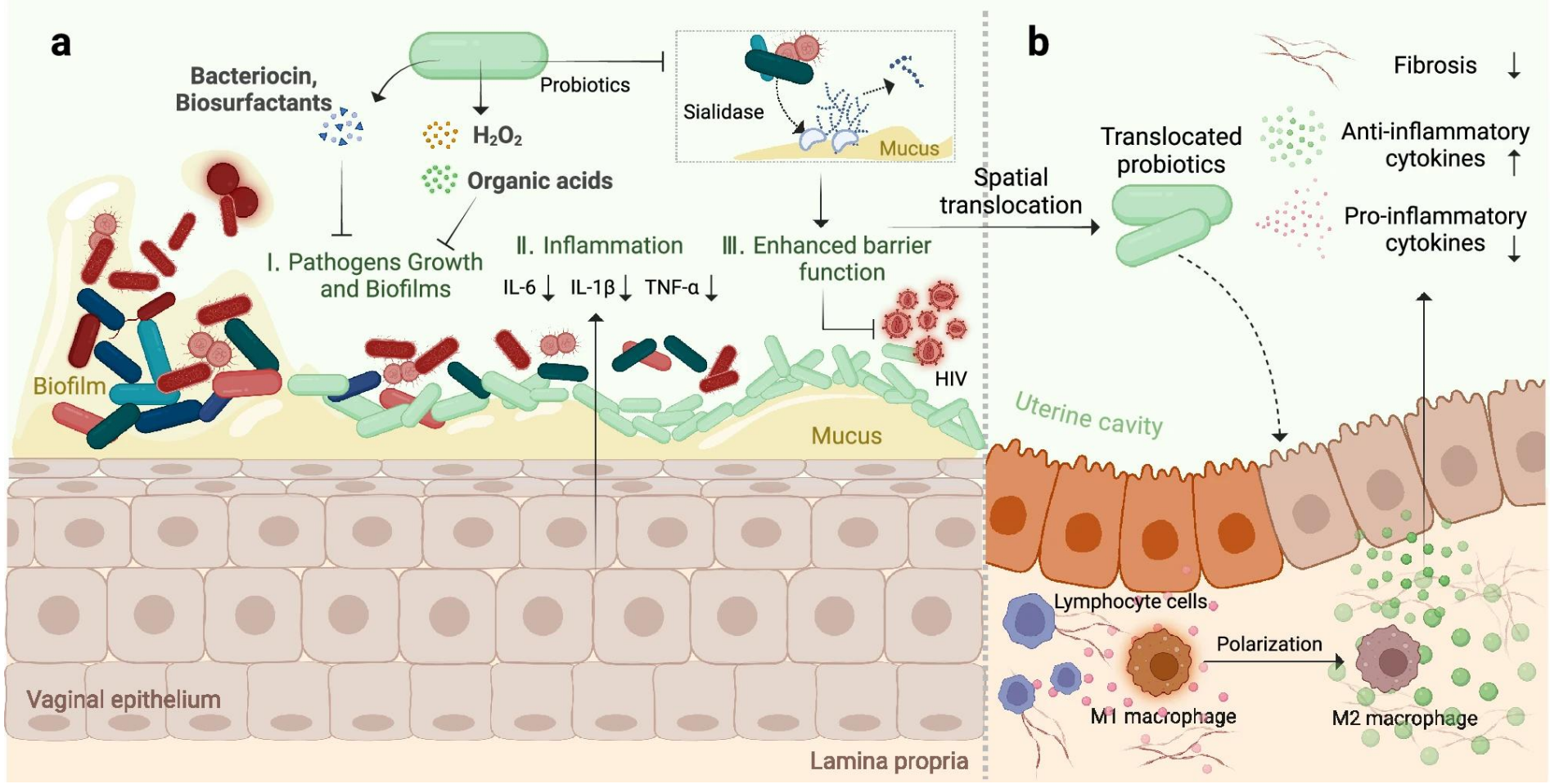


Vaginal suppositories

Probiotics potential in the vaginal niche



Cheng et al, 2025 npj Biofilms and Microbiome

Microbiome Center vaginal suppositories

Contains three active strains:

- *Lactobacillus crispatus* SP28 ($2.5x10^9$ cfu/piece)
- *Lactobacillus crispatus* LCR01 ($2.5x10^9$ cfu/piece)
- *Lactobacillus acidophilus* La02 ($2.5x10^9$ cfu/piece)

Matrix from cacao butter with coconut butter.

Available as 30 vaginal suppositories for EUR 81 (excluding VAT and transport)

Includes leaflet with clear instructions

Case report 1: post-menopausal

Woman, 75 years old

- Recurrent UTIs: complaints of dry vagina, slight burning sensation vagina (not when urinating), dyspareunia, urine stick nitrite pos
- Bowel: flatulence, diarrhea, histamine symptoms (headache, fuzzy, tired).
- Treatment: vitC, cranberry, D-mannose, solidago.
- Gut microbiome: MyOwnBlend after which bowels improved (headache and fatigue were gone) but vaginal complaints not yet.

- Vaginal microbiome analysis requested.
- Awaiting results: Vagifem (estrogens), probiofem Bonusan inserted vaginally.
- Results analysis.

Datum monsterafname	14.09.2022 00:00 AB	Gevalideerd door	Thomas Gugerel	Uitslagstatus	**Eindbericht**
Materiaal		Gevalideerd op	22.09.2022	Uitslagstatus op	22.09.2022

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Vaginaal diagnostiek				
Vaginaal microbioom				
Kenmerken van vaginale afscheiding				
pH-waarde	7,0		4,0 - 4,4	
Diversiteit				
Diversiteit	4,55		< 0,90	

De diversiteit in de vaginale microbiota kan van mens tot mens verschillen. Een lage diversiteit s is een teken van een gezonde fysiologische vaginale microbiota. Een hoge diversiteit kan op mycoses, pathogene bacteriën of seksueel overdraagbare aandoeningen wijzen.

Grad **4,5**

Vagina type / Community state type (CST)

De samenstelling van de vaginale microbiota kan in verschillende groepen verdeeld worden, de zogenaamde vagitypen. De vijf vagitypes I, II, III, IV en V worden onderscheiden door de dominerende lactobacillus species.

Vaginaltyp **IV**

Bacteriële vaginose-score

< 5

Aan de hand van de BV-score wordt de vaginale microbiota beoordeeld op een bacteriële vaginose (BV). Voor deze beoordeling wort gekeken naar de fysiologische lactobacillen flora, de anaerobe begeleidende flora en de BV-geassocieerde flora.

BV Score **8**

< 5 normaal
5 - 8 intermediair
> 8 positief

H2O2-opbouw				
H2O2 synthese index	1,00		> 4	
Lactobacillus (meest voorkomende spp.)				
Lactobacillus crispatus	0,00	%		
Lactobacillus gasseri	0,00	%		
Lactobacillus jensenii	0,00	%		
Lactobacillus iners	0,00	%		
Lactobacillus (totaal)	0,0	%	> 70,0	

AB=Abstrich *Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center . NL-. . Seite 1 von 2

Voornaam Denise Geslacht Vrouwelijk Ingangsdatum 14.09.2022

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Bacteriën geassocieerd met bacteriële vaginose				
Atopobium vaginae	0,00	%	< 0,01	
BVAB*-1	0,00	%	< 0,01	
BVAB*-2	0,00	%	< 0,01	
BVAB*-3	0,00	%	< 0,01	
Bacteroides fragilis	0,00	%	< 0,01	
Gardnerella vaginalis	0,00	%	< 0,01	
Megasphaera spp.	0,00	%	< 0,01	
Eggerthella spp.	0,00	%	< 0,01	
Aerococcus christensenii	0,00	%	< 0,01	
Dialister micraerophilus	0,55	%	< 0,01	
Prevotella spp.	23,03	%	< 0,01	
Dialister invisus	0,55	%	< 0,01	
Mobiluncus spp.	0,00	%	< 0,01	
Anaërobe bacteriën				
Anaerococcus spp.	14,17	%	< 0,01	
Bacteroides spp.	12,10	%	< 0,01	
Corynebacterium spp.	4,68	%	< 0,01	
Escherichia spp.	12,02	%	< 0,01	
Finegoldia spp.	2,09	%	< 0,01	
Gemella spp.	0,00	%	< 0,01	
Lachnospiraceae	0,60	%	< 0,01	
Mycoplasma spp.	0,00	%	< 0,01	
Parvimonas spp.	0,00	%	< 0,01	
Sneathia spp.	0,00	%	< 0,01	
Streptococcus spp.	0,00	%	< 0,01	
Ureaplasma spp.	0,00	%	< 0,01	
Veillonella spp.	0,00	%	< 0,01	
Overig	30,16	%		
Candidiasis				
Candida albicans	negatief		negatief	
Candida dubliniensis	negatief		negatief	
Candida glabrata	negatief		negatief	
Candida krusei	negatief		negatief	
Candida lusitaniae	negatief		negatief	
Candida parapsilosis	negatief		negatief	
Candida tropicalis	negatief		negatief	

AB=Abstrich *Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center . NL-. . Seite 2 von 2

Case report 1: post-menopausal

- Started MC vaginal suppositories
- Feels almost normal now, almost no more complaints vaginally.
- Personally feels suppositories have done a lot.

- Repeat measurement

Datum monsterafname	10.02.2023 00:00	Gevalideerd door	Dr. med. univ. Vilmos Fux	Uitslagstatus	**Eindbericht**
Materiaal	AB	Gevalideerd op	20.02.2023	Uitslagstatus op	20.02.2023

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Vaginaal diagnostiek				
Vaginaal microbioom				
Kenmerken van vaginale afscheiding				
pH-waarde	4,4		4,0 - 4,4	7,0
Diversiteit				
Diversiteit	0,15		< 0,90	4,55
				4,5

De diversiteit in de vaginale microbiota kan van mens tot mens verschillen. Een lage diversiteit s is een teken van een gezonde fysiologische vaginale microbiota. Een hoge diversiteit kan op mycoses, pathogene bacteriën of seksueel overdraagbare aandoeningen wijzen.

Grad **0,1**

Vagina type / Community state type (CST)

IV

De samenstelling van de vaginale microbiota kan in verschillende groepen verdeeld worden, de zogenaamde vagitypen. De vijf vagitypes I, II, III, IV en V worden onderscheiden door de dominerende lactobacillus species.

Vaginaltyp **I**

Bacteriële vaginose-score

< 5 — 8

Aan de hand van de BV-score wordt de vaginale microbiota beoordeeld op een bacteriële vaginose (BV). Voor deze beoordeling wort gekeken naar de fysiologische lactobacillen flora, de anaerobe begeleidende flora en de BV-geassocieerde flora.

BV Score **4**

< 5 normaal
5 - 8 intermediair
> 8 positief

H2O2-opbouw				
H2O2 synthese index	6,00		> 4	1,00
Lactobacillus (meest voorkomende spp.)				
Lactobacillus crispatus	98,92	%		0,00
Lactobacillus gasseri	0,00	%		0,00
Lactobacillus jensenii	0,00	%		0,00
Lactobacillus iners	0,00	%		0,00
Lactobacillus (totaal)	98,9	%	> 70,0	0,0

AB=Abstrich

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Bacteriën geassocieerd met bacteriële vaginose				
Atopobium vaginae	0,00	%	< 0,01	0,00
BVAB*-1	0,00	%	< 0,01	0,00
BVAB*-2	0,00	%	< 0,01	0,00
BVAB*-3	0,00	%	< 0,01	0,00
Bacteroides fragilis	0,00	%	< 0,01	0,00
Gardnerella vaginalis	0,00	%	< 0,01	0,00
Megasphaera spp.	0,00	%	< 0,01	0,00
Eggerthella spp.	0,00	%	< 0,01	0,00
Aerococcus christensenii	0,00	%	< 0,01	0,00
Dialister micraerophilus	0,01	%	< 0,01	0,55
Prevotella spp.	0,04	%	< 0,01	23,03
Dialister invisus	0,01	%	< 0,01	0,55
Mobiluncus spp.	0,00	%	< 0,01	0,00
Anaërobe bacteriën				
Anaerococcus spp.	0,20	%	< 0,01	14,17
Bacteroides spp.	0,00	%	< 0,01	12,10
Corynebacterium spp.	0,00	%	< 0,01	4,68
Escherichia spp.	0,00	%	< 0,01	12,02
Finegoldia spp.	0,02	%	< 0,01	2,09
Gemella spp.	0,00	%	< 0,01	0,00
Lachnospiraceae	0,00	%	< 0,01	0,60
Mycoplasma spp.	0,00	%	< 0,01	0,00
Parvimonas spp.	0,00	%	< 0,01	0,00
Sneathia spp.	0,00	%	< 0,01	0,00
Streptococcus spp.	0,00	%	< 0,01	0,00
Ureaplasma spp.	0,00	%	< 0,01	0,00
Veillonella spp.	0,00	%	< 0,01	0,00
Overig	0,81	%		30,16
Candidiasis				
Candida albicans	negatief		negatief	negativ
Candida dubliniensis	negatief		negatief	negativ
Candida glabrata	negatief		negatief	negativ
Candida krusei	negatief		negatief	negativ
Candida lusitaniae	negatief		negatief	negativ
Candida parapsilosis	negatief		negatief	negativ
Candida tropicalis	negatief		negatief	negativ

AB=Abstrich

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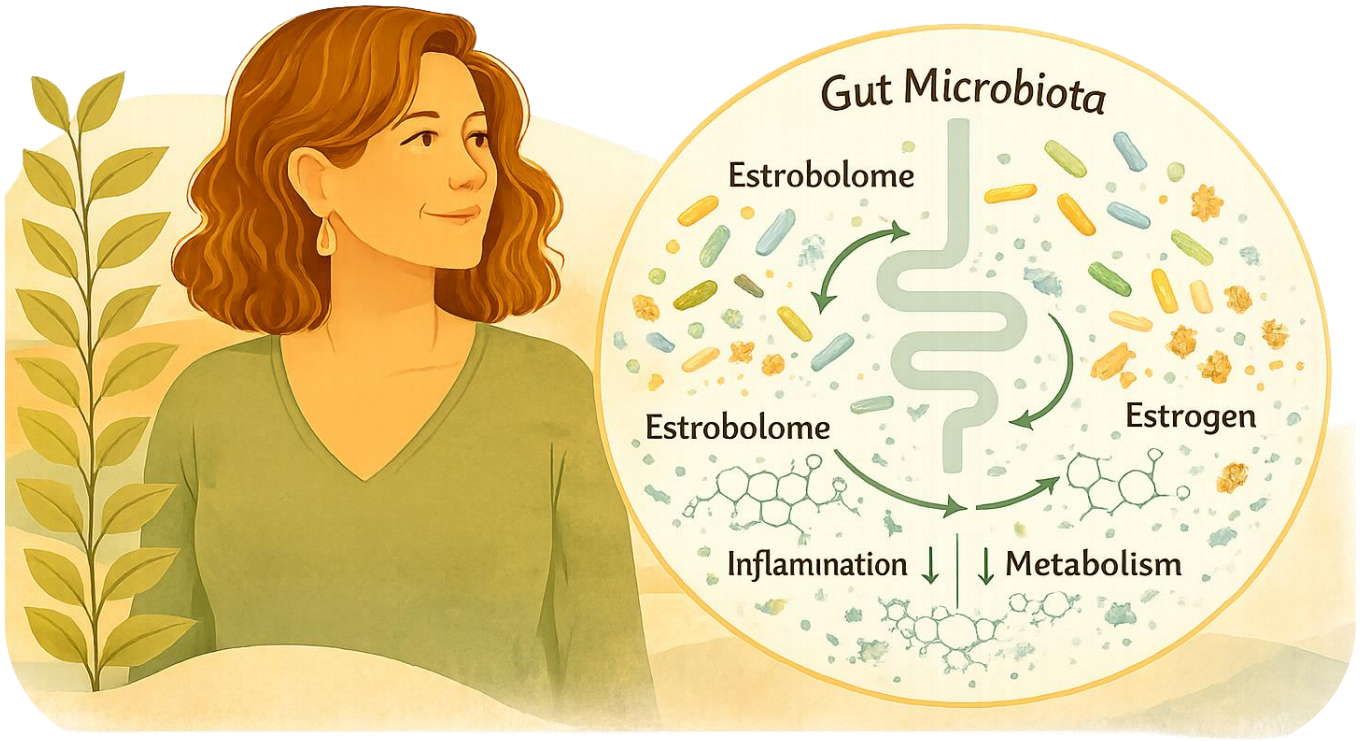


Gut Microbiota during menopause

Why look beyond the vagina?

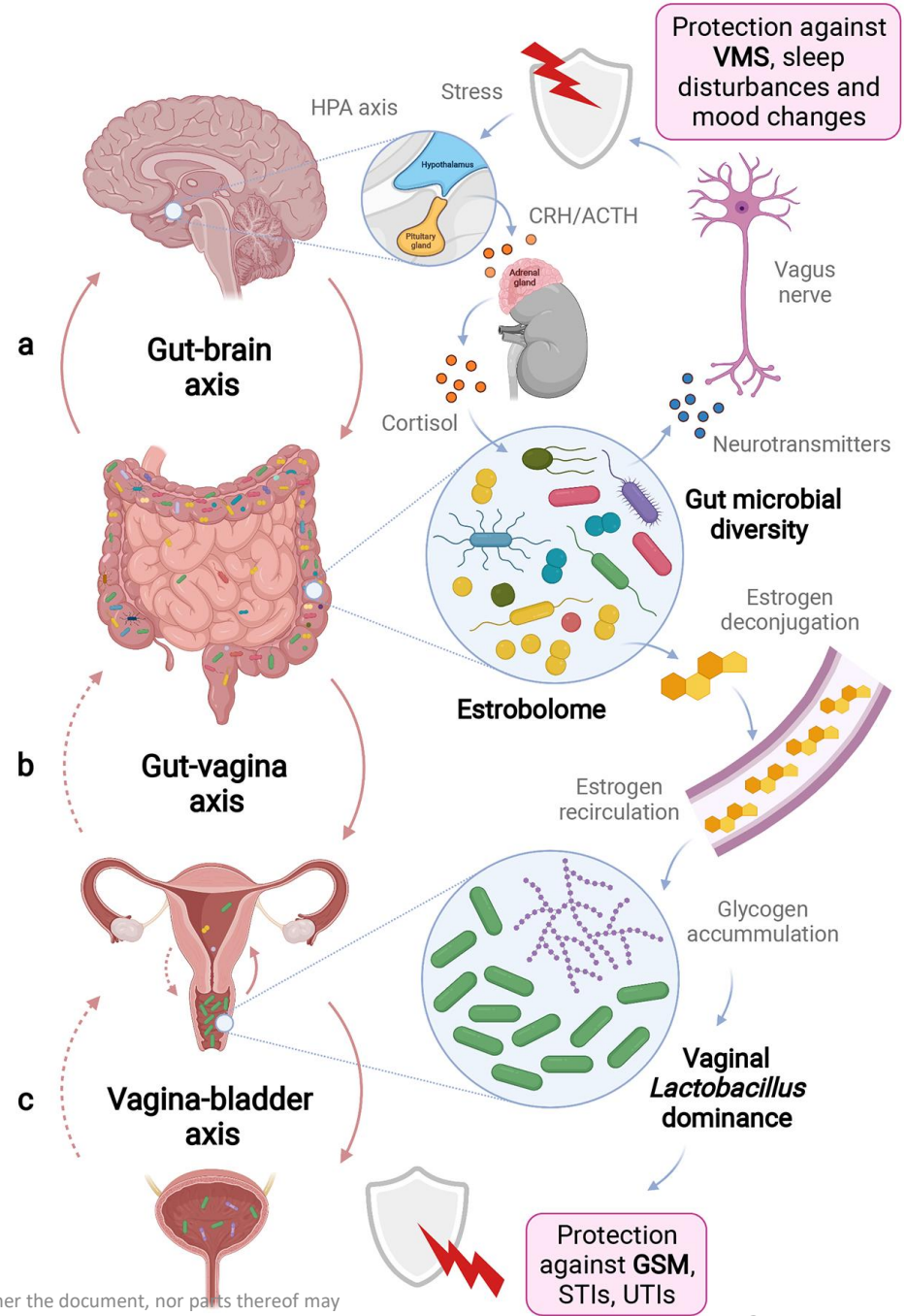
Menopause is a systemic transition, and the gut microbiota may contribute to symptom development

During menopause estrogen decline affecting multiple body systems

Gut microbiota interact with:

- estrogen metabolism
- inflammation
- metabolism
- brain signaling

Emerging concept: gut–brain–vagina axis – help maintain systemic and urogenital health in ageing women.



1. Laniewski et al 2022 Nat Microbiol doi: 10.1038/s41564-022-01071-6

Menopause alter the gut microbiota composition

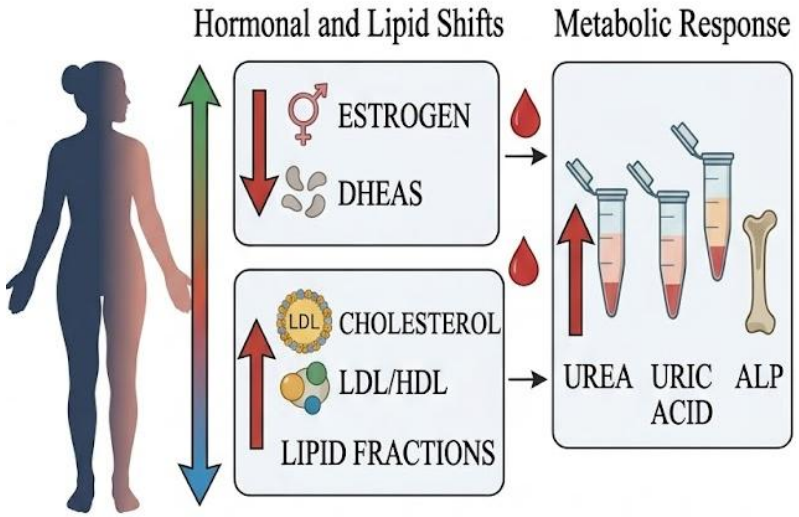
Target microbiome studies suggest menopause is associated with shifts in gut bacterial composition and correlations with hormonal and metabolic markers, supporting a gut–endocrine interaction model.

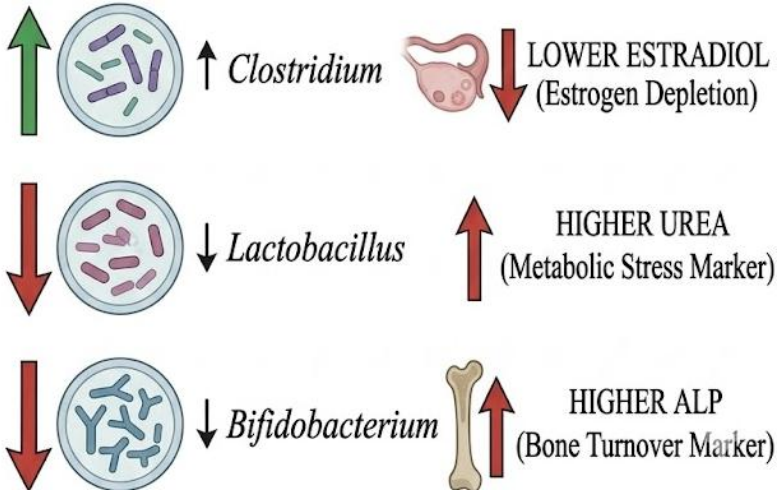
Menopause transition was associated with:

- ↑ cholesterol and lipid changes
- ↑ metabolic markers (urea, uric acid, ALP)
- hormonal decline (estrogen, DHEAS trends)

In postmenopausal women

- ↑ *Clostridium* was associated with lower estradiol levels, suggesting an estrogen depletion
- ↓ *Lactobacillus* was associated with higher urea - metabolic stress marker
- ↓ *Bifidobacterium* was associated with bone turnover marker (ALP)





1. de Silva et al., 2022 BMC Women's Health https://doi.org/10.1186/s12905-022-02063-8

Gut microbiota and metabolomics in postmenopausal women

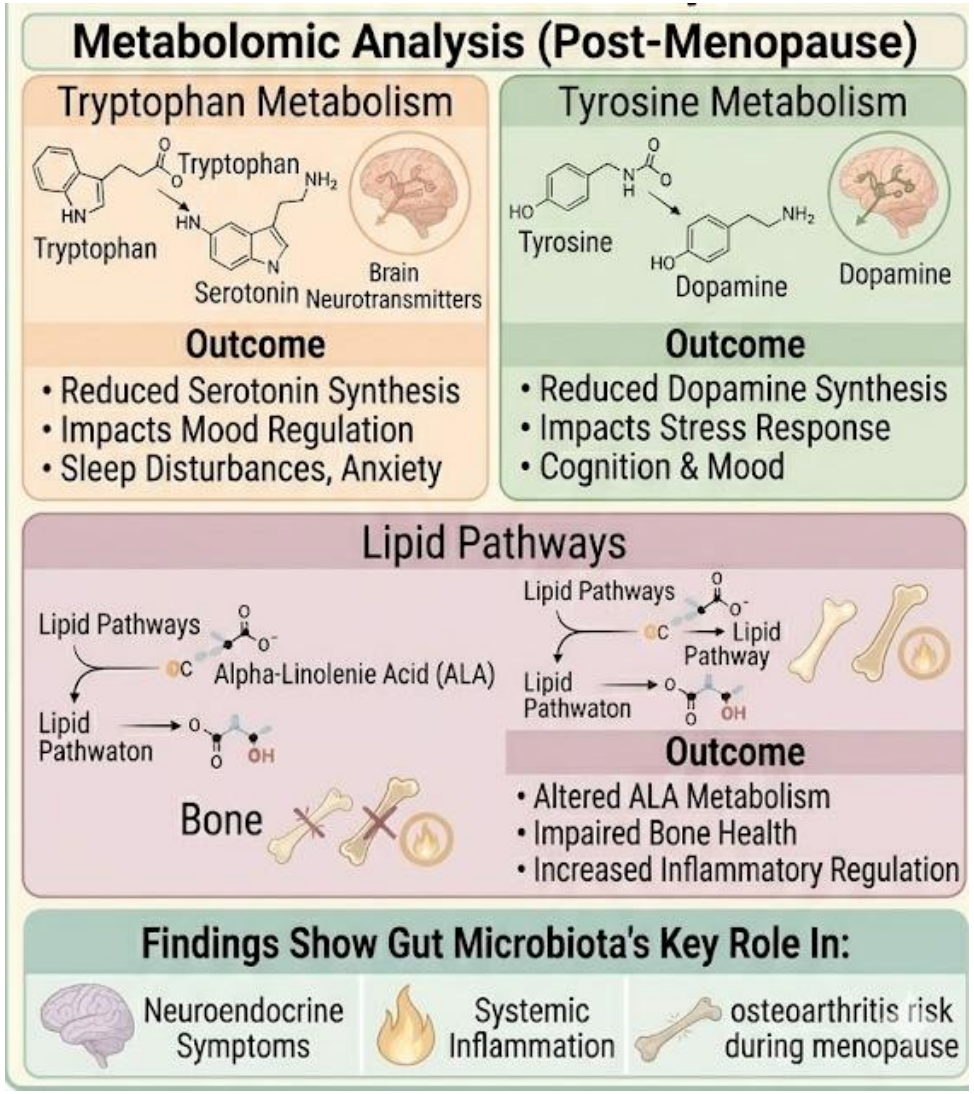
Menopause-associated hormonal changes were linked to altered gut microbiota composition, linked to SCFAs production

Women with higher Follicle-Stimulating Hormone (FSH) more commonly reported hot flashes, sweating and bone pain.

Metabolomic analysis showed alterations in **stool** levels of:

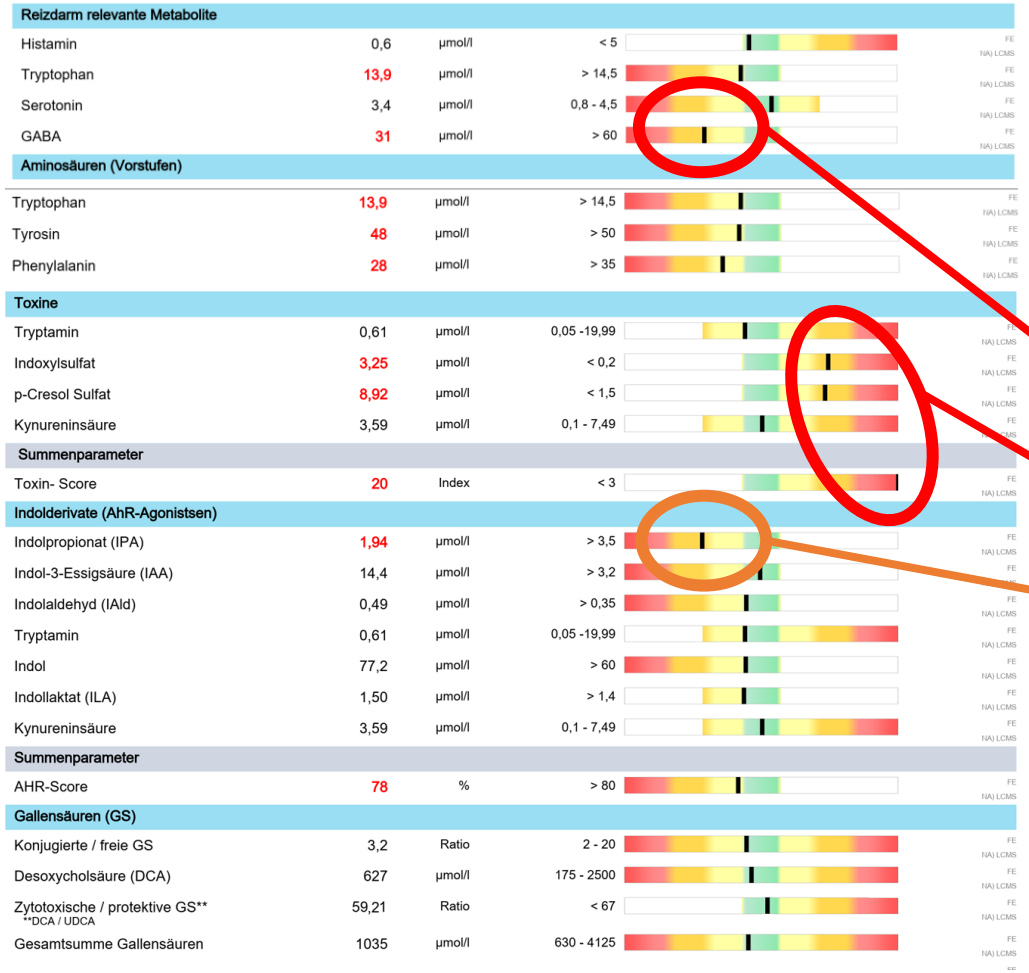
- tryptophan metabolites
- tyrosine metabolites
- lipid metabolites

Rational to include metabolites analysis for women during perimenopause and postmenopause



1. Xie et al., 2024 BMC Women's Health https://doi.org/10.1186/s12905-024-03448-7

The advice aid contains an easy way to use the metabolome data



Reizdarm relevante Metabolite			
Histamin	0,6	µmol/l	< 5
Tryptophan	13,9	µmol/l	> 14,5
Serotonin	3,4	µmol/l	0,8 - 4,5
GABA	31	µmol/l	> 60
Aminosäuren (Vorstufen)			
Tryptophan	13,9	µmol/l	> 14,5
Tyrosin	48	µmol/l	> 50
Phenylalanin	28	µmol/l	> 35
Toxine			
Tryptamin	0,61	µmol/l	0,05 -19,99
Indoxylsulfat	3,25	µmol/l	< 0,2
p-Cresol Sulfat	8,92	µmol/l	< 1,5
Kynureninsäure	3,59	µmol/l	0,1 - 7,49
Summenparameter			
Toxin- Score	20	Index	< 3
Indolderivate (AhR-Agonistsen)			
Indolpropionat (IPA)	1,94	µmol/l	> 3,5
Indol-3-Essigsäure (IAA)	14,4	µmol/l	> 3,2
Indolaldehyd (IAld)	0,49	µmol/l	> 0,35
Tryptamin	0,61	µmol/l	0,05 -19,99
Indol	77,2	µmol/l	> 60
Indollaktat (ILA)	1,50	µmol/l	> 1,4
Kynureninsäure	3,59	µmol/l	0,1 - 7,49
Summenparameter			
AHR-Score	78	%	> 80
Gallensäuren (GS)			
Konjugierte / freie GS	3,2	Ratio	2 - 20
Desoxycholsäure (DCA)	627	µmol/l	175 - 2500
Zytotoxische / protektive GS** **DCA / UDCA	59,21	Ratio	< 67
Gesamtsumme Gallensäuren	1035	µmol/l	630 - 4125

Metabolome (6)

Erhöhtes Histamin	0	Liegt in der Metabolomanalyse ein erhöhter Histaminspiegel vor? 0 = Keine Erhöhung; 1 = ein bisschen; 2 = Erhöhung; 3 = starke Erhöhung; 4 = sehr starke Erhöhung.
Erniedrigtes Serotonin	0	Liegt in der Metabolomanalyse ein erniedrigter Serotoninspiegel vor? 0 = keine Erniedrigung; 1 = ein bisschen; 2 = Erniedrigt; 3 = stark erniedrigt; 4 = sehr stark erniedrigt.
Erhöhtes serotonine	0	Liegt in der Metabolomanalyse ein erhöhter Serotoninspiegel vor? 0 = Keine Erhöhung; 1 = ein bisschen; 2 = Erhöhung; 3 = starke Erhöhung; 4 = sehr starke Erhöhung.
Erniedrigtes GABA	2	Liegt in der Metabolomanalyse ein erniedrigter GABA-spiegel vor? 0 = keine Erniedrigung; 1 = ein bisschen; 2 = Erniedrigt; 3 = stark erniedrigt; 4 = sehr stark erniedrigt.
Erhöhte toxische Metaboliten	3	Liegen in der Metabolomanalyse erhöhte toxische Metaboliten vor? 0 = Keine Erhöhung; 1 = ein bisschen; 2 = Erhöhung; 3 = starke Erhöhung; 4 = sehr starke Erhöhung.
Ungleichgewicht der AhR-Agonisten	1	Liegt in der Metabolomanalyse ein Ungleichgewicht der AhR-Agonisten vor? Dies kann auftreten bei erniedrigtem IPA, IAA, IAld, Indol oder ILA, erhöhtem Tryptamin oder Kynurensäure, oder in geringerem Maße bei erniedrigtem Tryptamin oder Kynurensäure. 0 = kein Ungleichgewicht; 1 = ein bisschen; 2 = Ungleichgewicht; 3 = starke Ungleichgewicht; 4 = sehr starke Ungleichgewicht.

The estrobolome – the link between the gut microbiota and estrogen

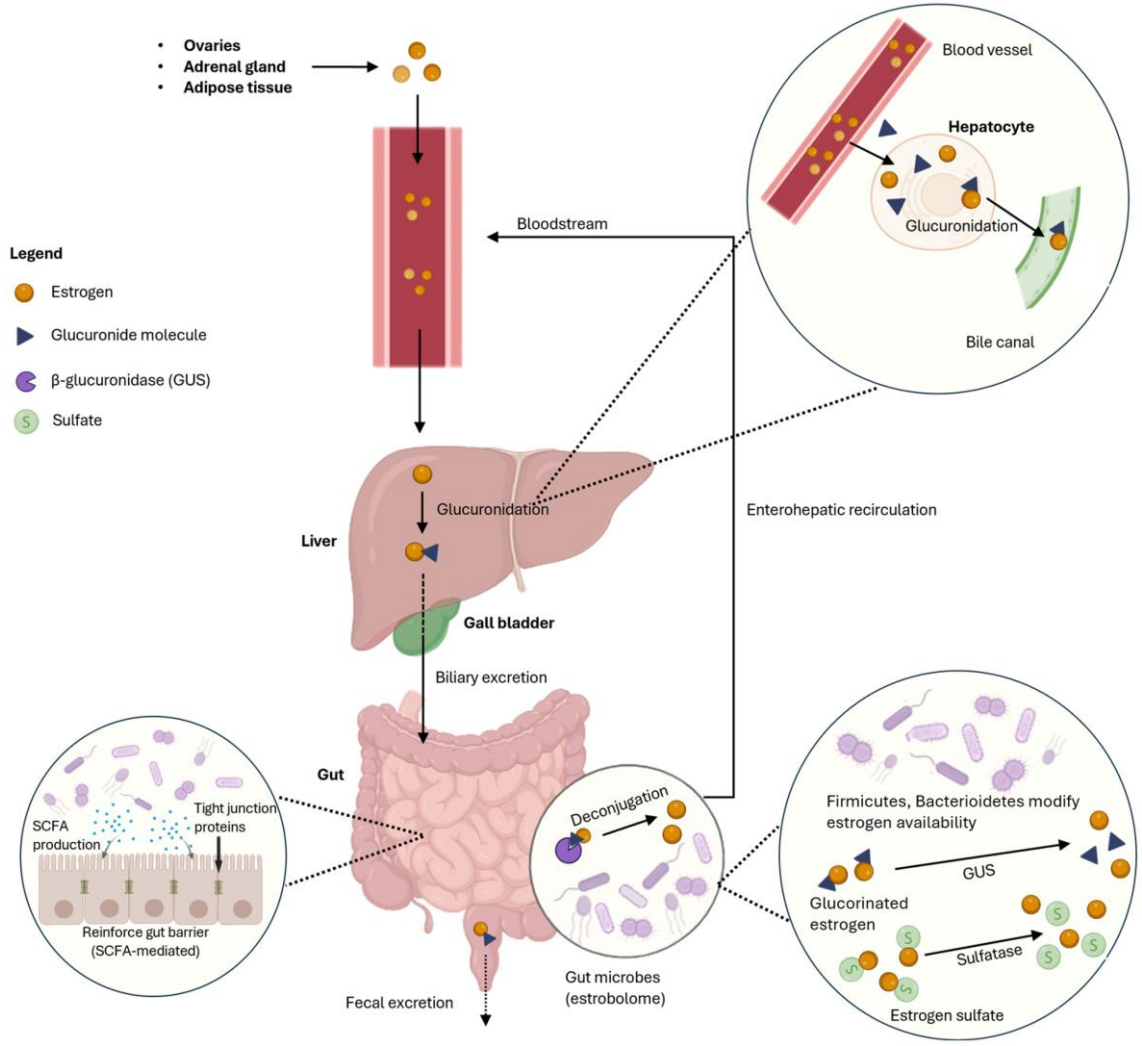
Liver → estrogens inactivated and excreted into the gut

Gut bacteria reactivate estrogens

- regulate if estrogen is eliminated or recycled
- recycling loop (enterohepatic circulation) is a major determinant of overall estrogen exposure

Active estrogens are reabsorbed into circulation and can bind to estrogen receptors in:

- Brain → mood, cognition
- Cardiovascular system → vascular function
- Metabolic tissues → insulin sensitivity
- Bone → inhibits bone resorption
- Vaginal epithelium → maintains tissue + microbiota

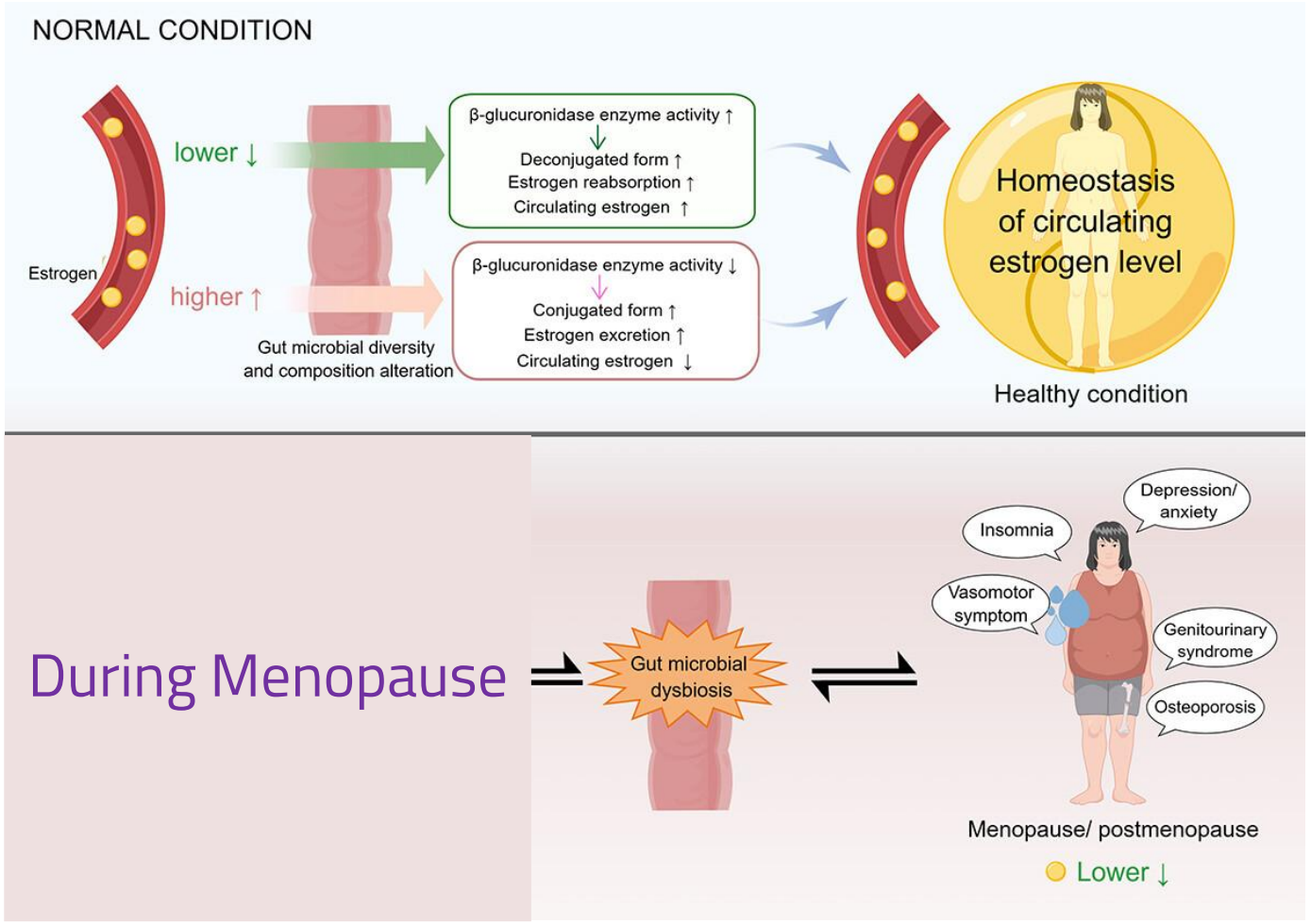


1. Lim et al., 2026 Nutrients https://doi.org/10.3390/nu18071052

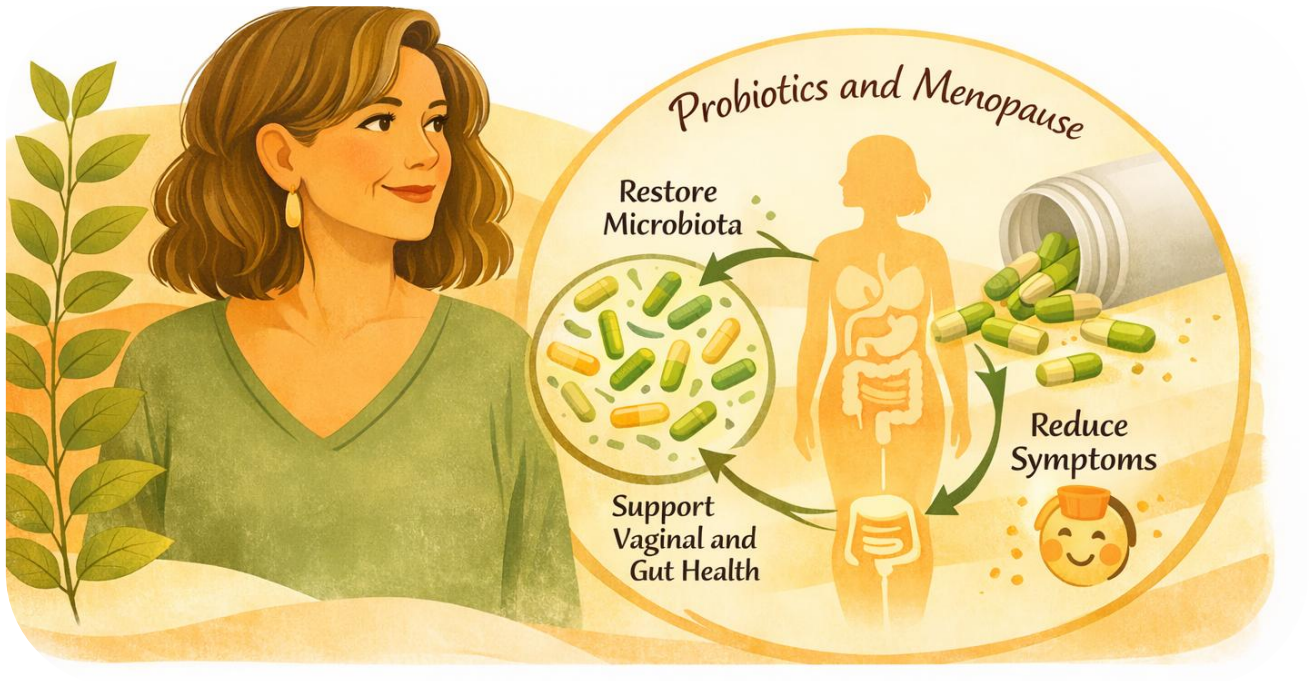
The estrobolome and menopause symptoms

Gut microbiota (the estrobolome) contribute to menopausal symptoms

- Vasomotor symptoms
- Mood/sleep
- Metabolic dysfunction
- Bone health
- Vaginal health (Genitourinary Syndrome of Menopause)



1. Hu et al., 2024 Gut Microbes https://doi.org/10.1080/19490976.2023.2236749

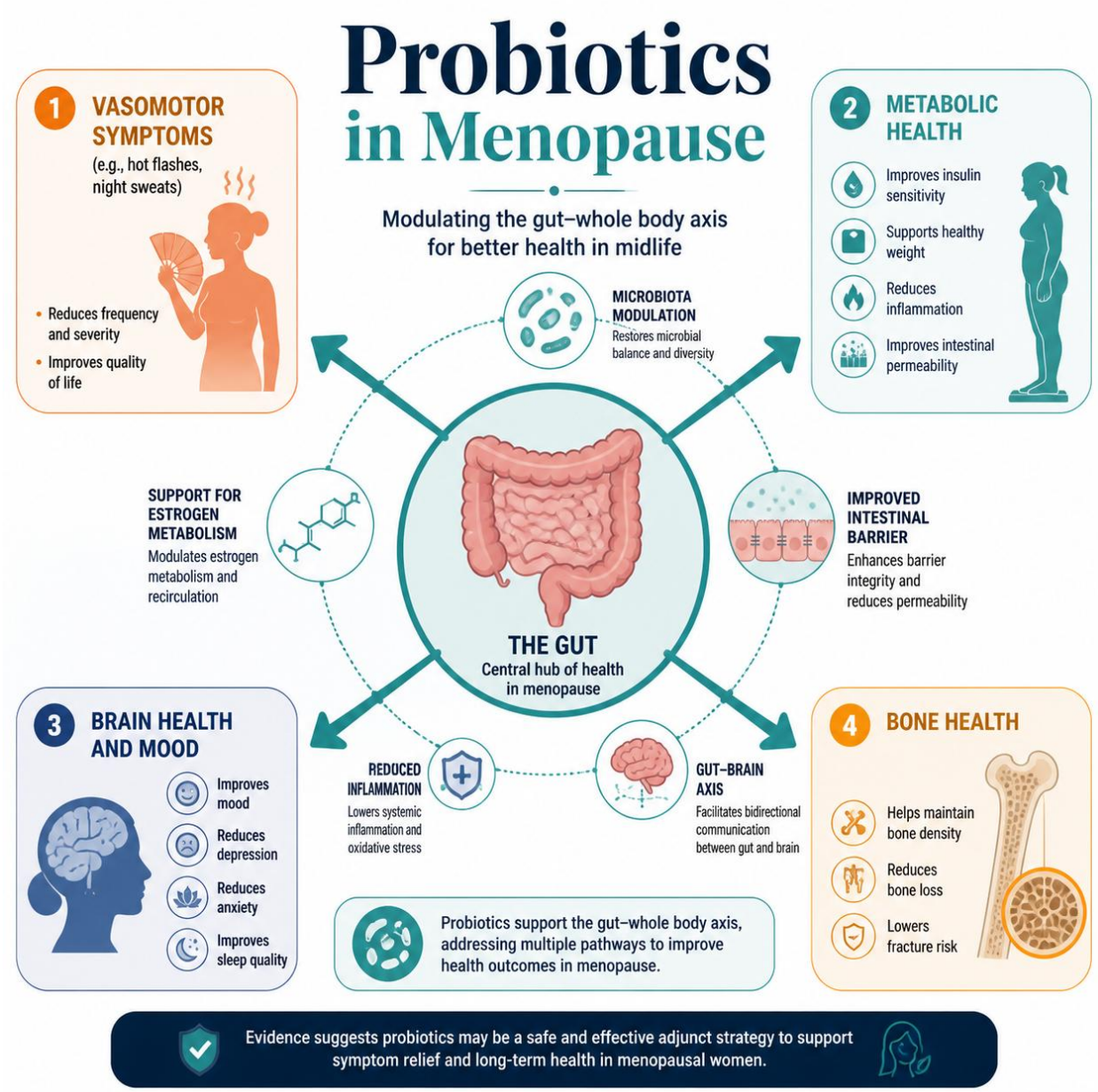


Oral probiotics targeting the gut during menopause

Probiotic Potential

Improve clinically relevant symptoms linked to menopause

- Vasomotor symptoms
- Metabolic Health
- Bone Health
- Brain Health
- Vaginal Health

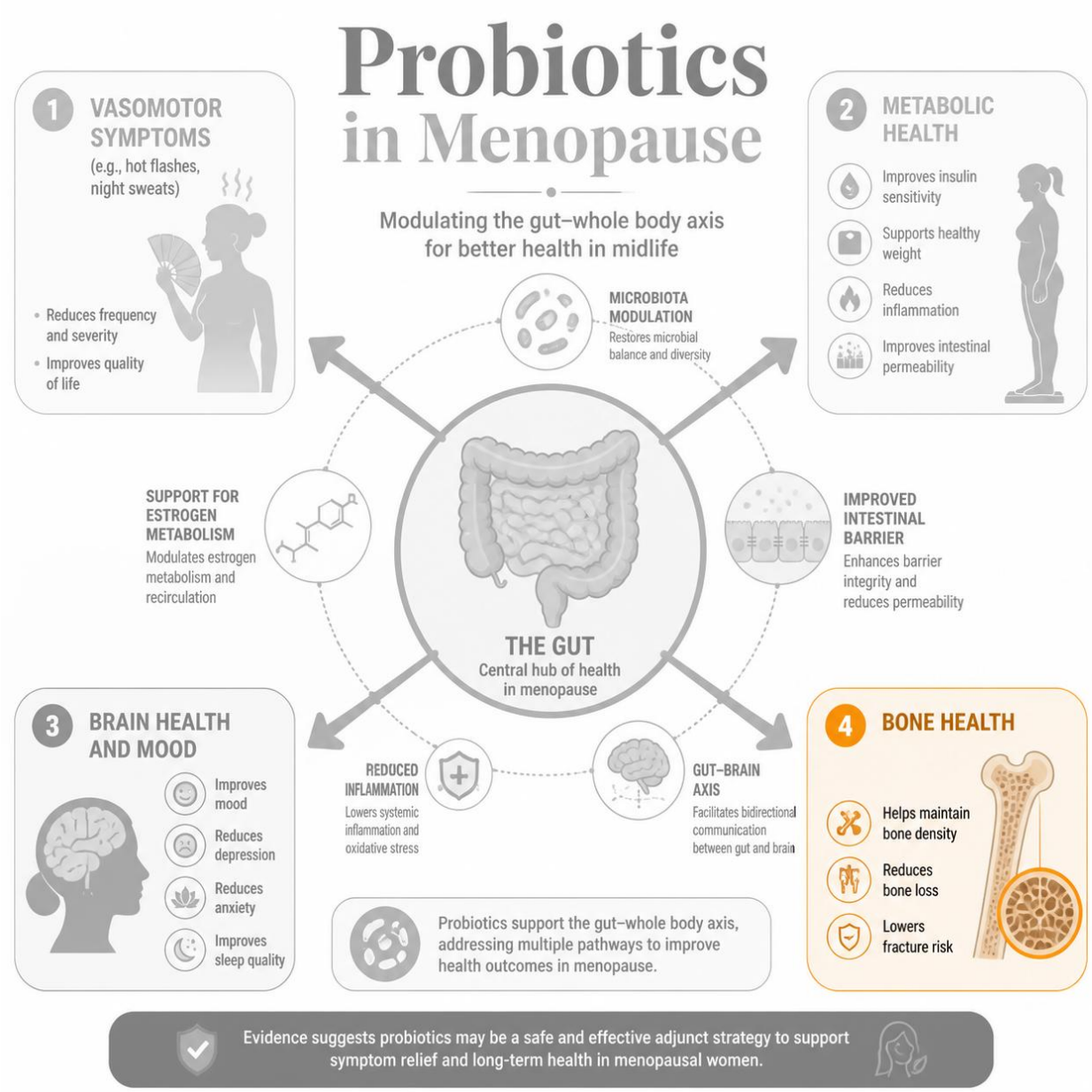


Microbiome Center

Probiotic Potential

Improve clinically relevant symptoms linked to menopause

- Vasomotor symptoms
- Metabolic Health
- **Bone Health**
- Brain Health
- Vaginal Health



Microbiome Center

Vitamin K2 booster

- This booster contains 4 strains:
  - *Lactobacillus brevis* W63,
  - *Bacillus coagulans* W64,
  - *Propionibacterium freundenreichii* W200,
  - *Bacillus subtilus* W201

- These strains are selected for their capacity to produce vitamin K2 in various subtypes (fig)[1].
- Vitamin K2 produced by bacteria in the gut can be absorbed and contributes to vitamin K2 use by other commensals[2,3].
- Evidence for therapeutic uses of vitamin K2:
  - **Osteoporosis (meta-analysis of RCTs, fig)4**
  - Arterial stiffness[5]
  - Glycemic control / T2DM[6-8]
  - Depression[9]
- Typical use: patients with osteoporosis or atrial stiffness combined with metabolic dysfunction

	MK4	MK5	MK6	MK7	MK8	MK9	MK9-4H	MK10
B.subtilis W201		0,1	0,4	105,9	1,9	0,2		
P. freudenreichii W200		0,2		0,02	0,3	20,1	1040	
B. coagulans W64		0,1	0,1	23,7	1,3	0,1		0,1
L. brevis W63				0,01	0,004	0,007		

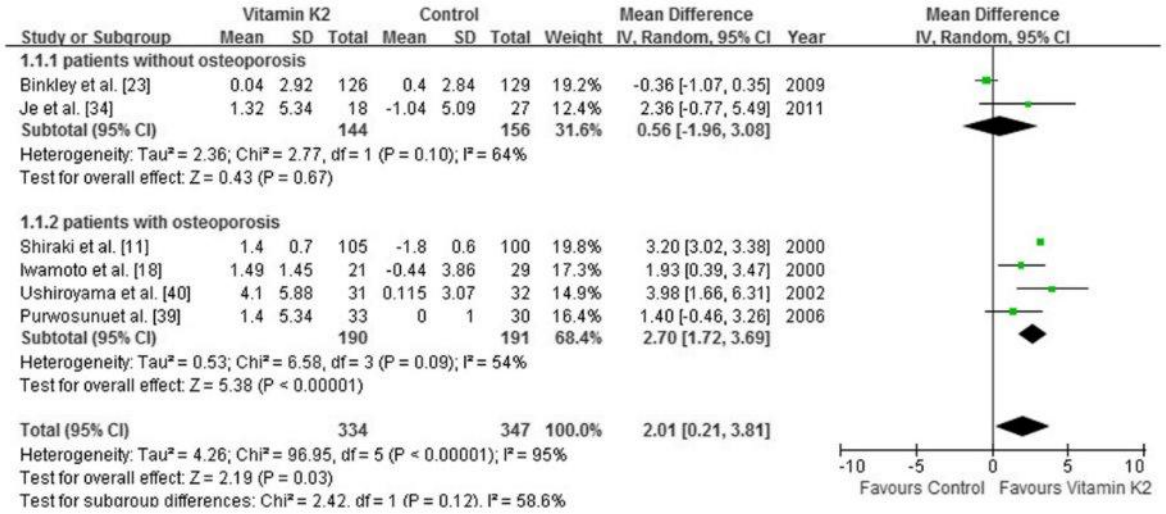


Fig. 2 Forest plot of the medium-term follow-up of vertebral BMD changes, showing a significant improvement of vertebral BMD in osteoporosis subgroup analysis and overall effect for vitamin K2 over control group

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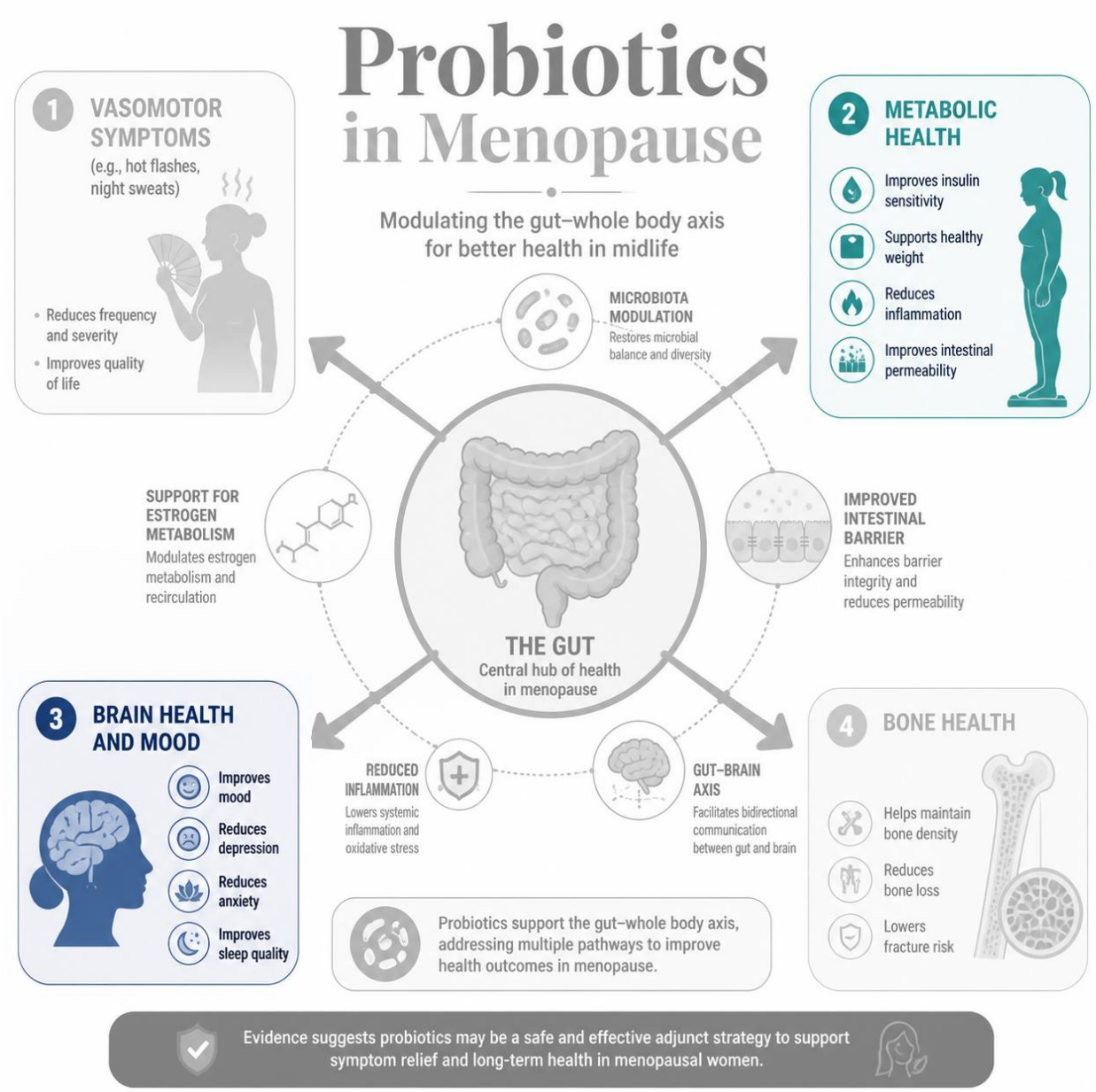
9. Tarkesh, F. et al. BMC Womens Health 22, 315 (2022)

Probiotic Potential

Improve clinically relevant symptoms linked to menopause

- Vasomotor symptoms
- **Metabolic Health**
- Bone Health
- **Brain Health**
- Vaginal Health



Microbiome Center

L. plantarum P-8

- The *Lactiplantibacillus plantarum* P-8 is isolated from a traditional fermented dairy product from Mongolia.
- A well-designed RCT shows an effect on **depression, stress and anxiety**[2], which is expected to be caused by changes in microbial production of neuro-active substances such as GABA[3].
- In addition, there is evidence for:
  - IBS[4]
  - Anti-inflammatory effect[4,2]
  - Increasing sIgA excretion[5]
  - Reduction of bile acids[5]

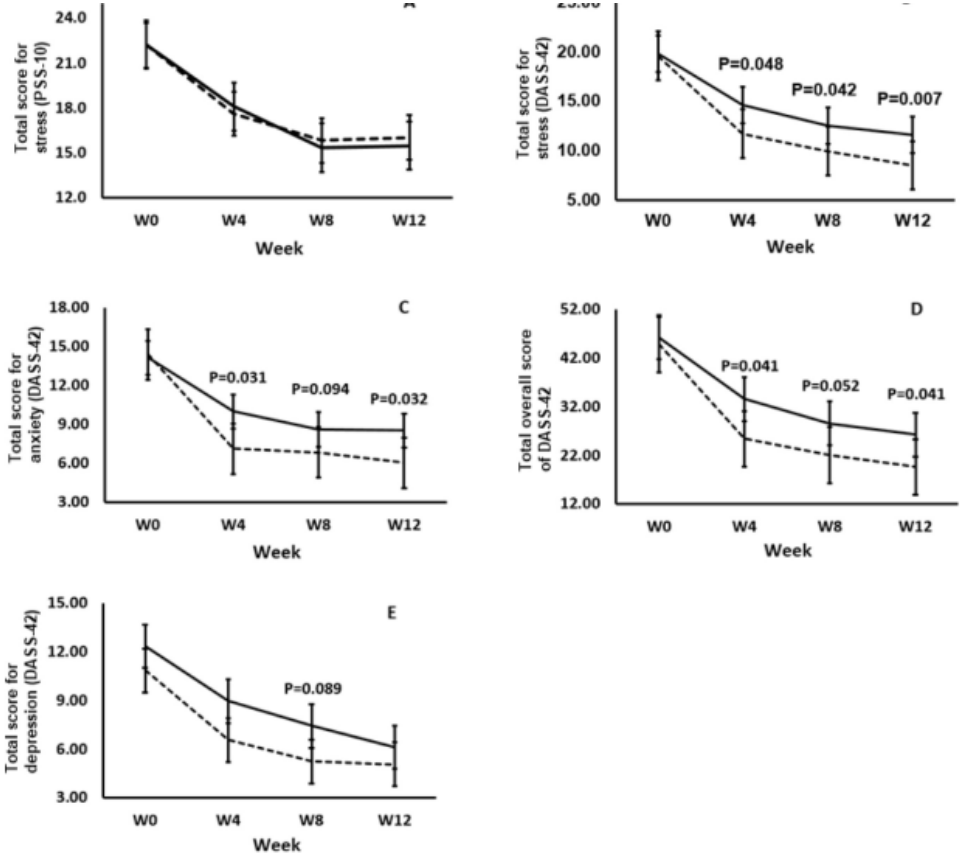


Fig. 2. Effects of a 12-week administration of probiotic *L. plantarum* P8, P8 (---) or placebo (—) on the total scores of (A) stress based on the PSS-10 questionnaire (W: $P < 0.001$, T: $P = 0.788$, TxW: $P = 0.820$), (B) stress (W: $P < 0.001$, T: $P = 0.030$, TxW: $P = 0.293$), (C) anxiety (W: $P < 0.001$, T: $P = 0.077$, TxW: $P = 0.170$), (D) total scores (W: $P < 0.001$, T: $P = 0.054$, TxW: $P = 0.427$), and (E) depression (W: $P < 0.001$, T: $P = 0.163$, TxW: $P = 0.787$) based on the DASS-42 questionnaire. P-values indicated difference between treatment groups at individual time points. Results are expressed as mean; error bars (SEM); n = 103. Repeated measures ANOVA provided statistical significance on W: effect of weeks; T: effect of treatment groups P8 and placebo; TxW: interaction between weeks and treatment.

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3. Ma, T. et al. Neurobiol Stress 14, 100294 (2021)
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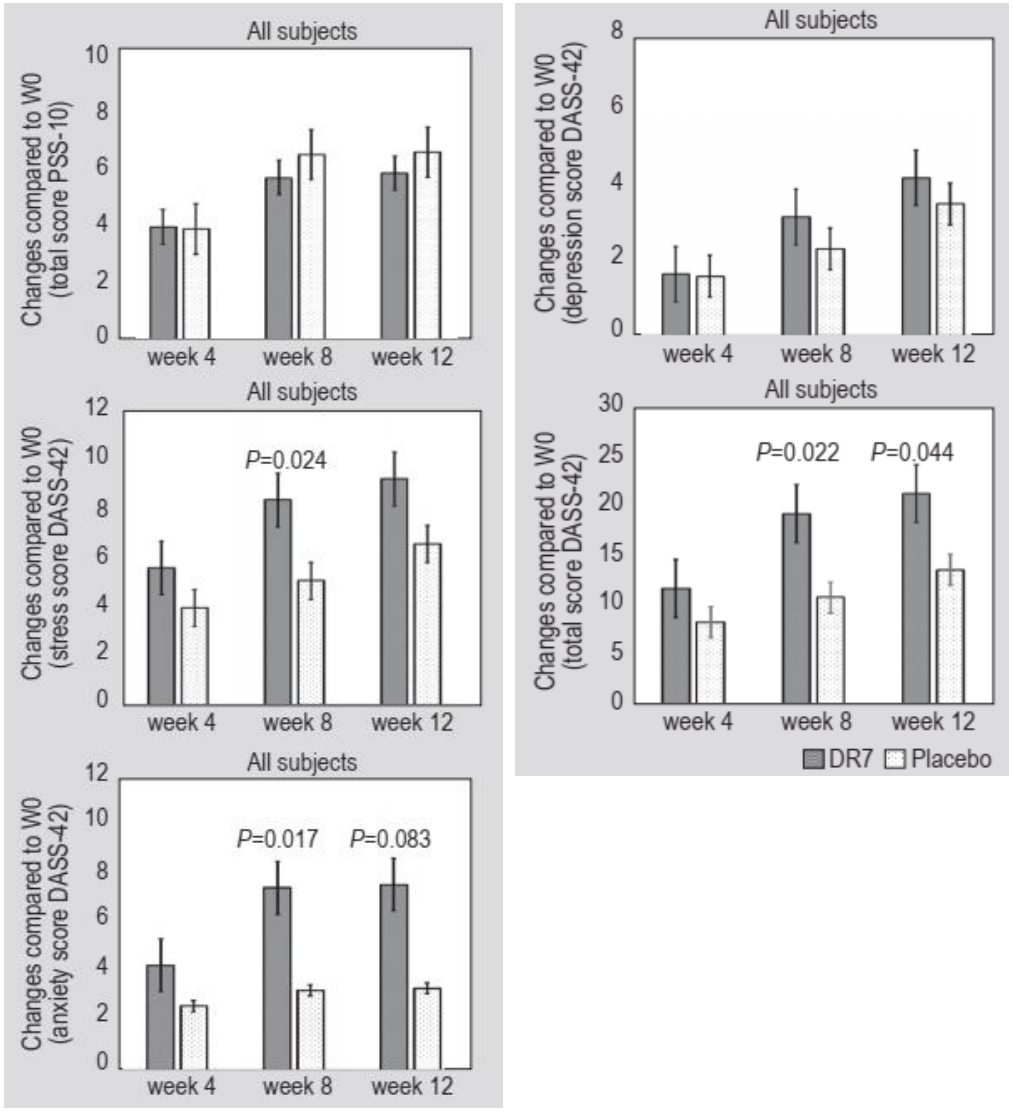
L. plantarum DR-7

- The *Lactiplantibacillus plantarum* DR-7 is isolated from fresh cow's milk in Malaysia[1].
- A well-designed RCT shows a convincing effect on **stress and anxiety**[2]. Mechanistic evidence suggests that this is induced **via pathways of serotonin** and oxidative ageing[3].
- In addition, based on metabolites analysis the and integration of Biovis metabolites measurements the strain can increase serotonin
- There is also evidence for:
  - Upper respiratory tract infections[4,5]
  - Anti-inflammatory effects[2-4]
  - **Increases AMPK activity**[1,6-8]



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6. Yap, P.-G. et al. Appl Biochem Biotechnol 191, 226–244 (2020)
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PHGG

- This fiber is derived from the guar bean (*Cyamopsis tetragonoloba*) and partially hydrolyzed enzymatically to make it less viscous[1].
- This fiber is extremely well-studied, hundreds of clinical studies have been conducted since 1970's.
- Different from most other fibers, PHGG has found to be efficacious at daily doses of ~5g.
- Important therapeutic uses:
  - **Insulin resistance (dozens of studies, fig[2,3,11])**
  - IBS, abdominal pain, bloating[1,4,5]
  - Constipation[6,7]
  - Diarrhea[8,9]
  - **Depression and anxiety[1]**
  - SIBO[10]
- Typical use: IBS and symptoms, SIBO, diabetes

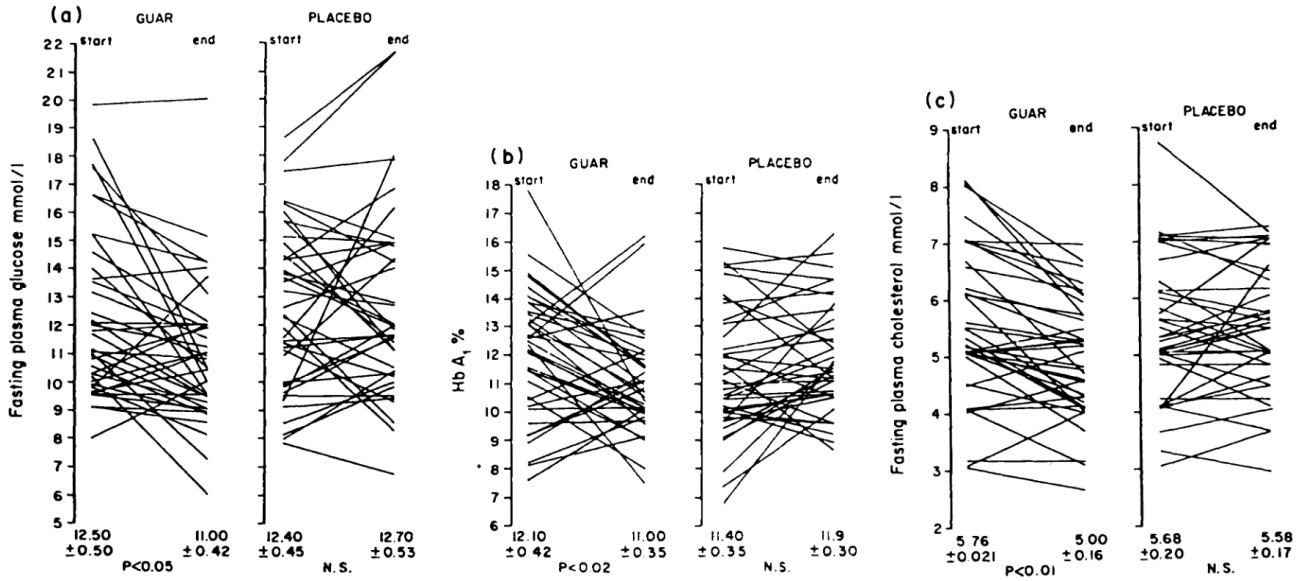

FIGURE 1. Individual changes in fasting plasma glucose (a), glycosylated hemoglobin (b), and cholesterol (c) in all 39 patients.

TABLE 3. *Clinical data on patients at the beginning and end of each treatment period.*

Clinical variables	Guar period			Placebo period		
	B	E	Significance	B	E	Significance
FPG (mmol/L)	12.50 ± 0.50	11.00 ± 0.42	$P < 0.05$	12.4 ± 0.45	12.7 ± 0.53	NS
HbAl (%)	12.10 ± 0.42	11.00 ± 0.35	$P < 0.02$	11.40 ± 0.35	11.90 ± 0.30	NS

1. Parisi, G. et al. Dig Dis Sci 50, 1107–1112 (2005)
2. Peterson, D. B. et al. Diabetic Medicine 4, 111–115 (1987)
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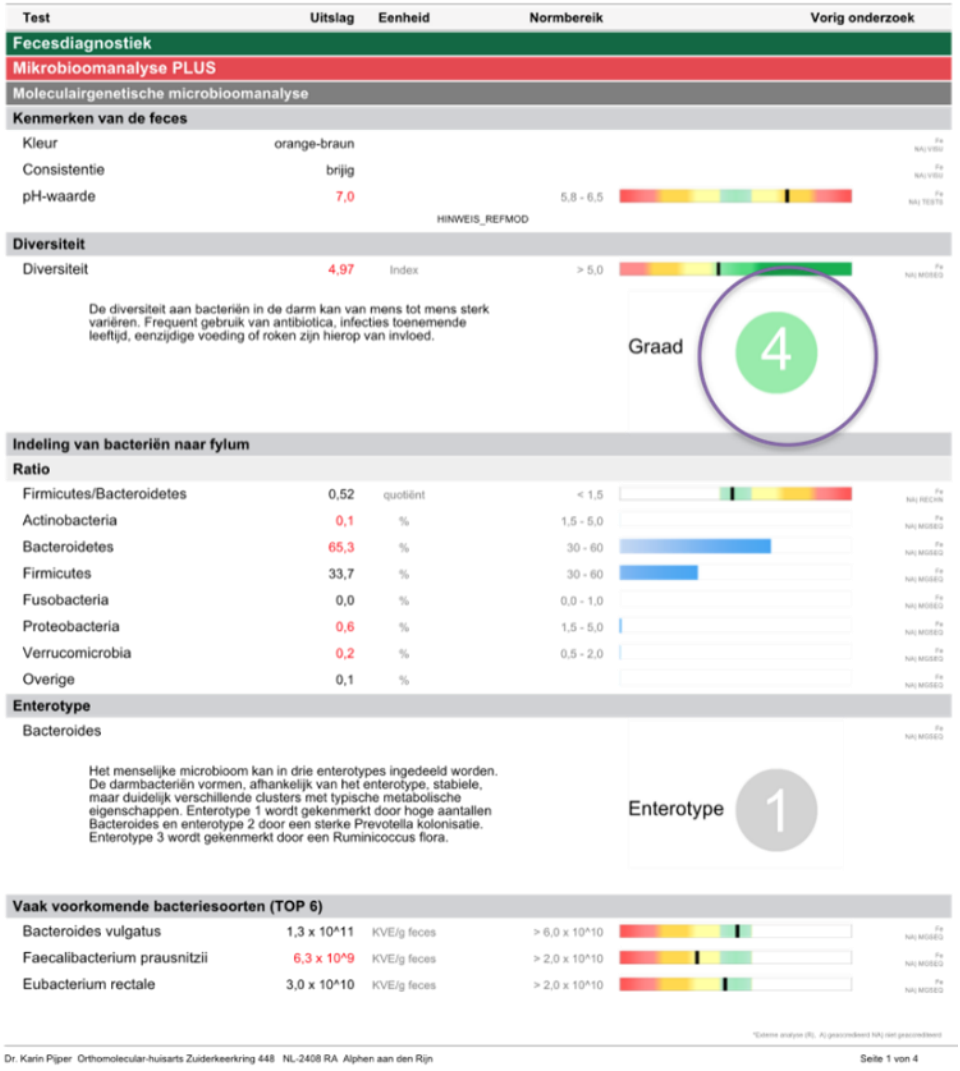
Case 2 Metabolic syndrome + depression

- Lady 60 y/o
- Obese (BMI 36)
- Fasting glucose 8.2, HbA1c 45
- Hypertension, kidney stones, UTIs, fatique
- Diverticulitis
- Hospitalized for dehydration
- Sad mood/anxiety/depression
- Medication: Citalopram 10mg, Enalapril 5mg
- Answered positive on every GI complaints question of the Microbiome Center questionnaire:
    - ➢ Abdominal pain, changing frequency, changing BSS type, bloating, belching, pain after meal, fatty stools, food intolerances, etc.

Case report 2 Metabolic syndrome + depression



Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Mikrobioomanalyse PLUS				
Moleculairgenetische microbioomanalyse				
Kenmerken van de feces				
Kleur	orange-braun			
Consistentie	brijig			
pH-waarde	7,0		5,8 - 6,5	
		HINWEIS_REFMOD		
Diversiteit				
Diversiteit	4,97	Index	> 5,0	

De diversiteit aan bacteriën in de darm kan van mens tot mens sterk variëren. Frequent gebruik van antibiotica, infecties toenemende leeftijd, eenzijdige voeding of roken zijn hierop van invloed.

Graad 4

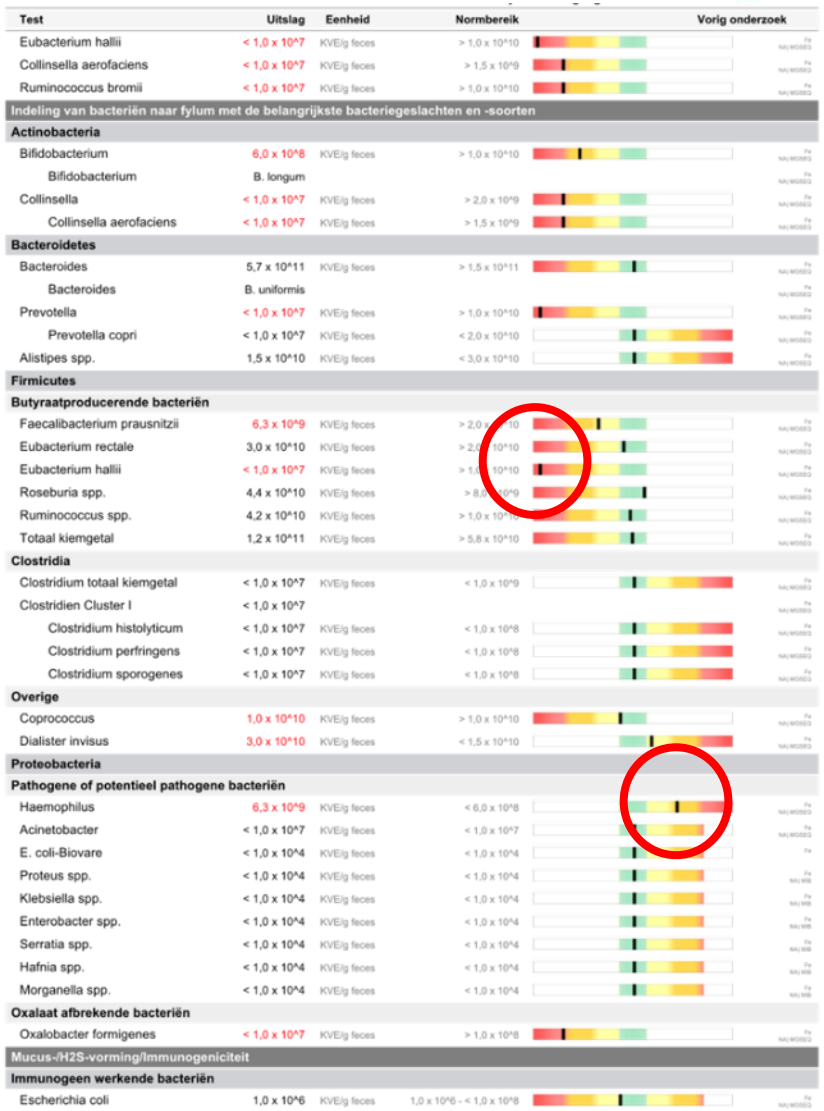
Indeling van bacteriën naar fylum				
Ratio				
Firmicutes/Bacteroidetes	0,52	quotiënt	< 1,5	
Actinobacteria	0,1	%	1,5 - 5,0	
Bacteroidetes	65,3	%	30 - 60	
Firmicutes	33,7	%	30 - 60	
Fusobacteria	0,0	%	0,0 - 1,0	
Proteobacteria	0,6	%	1,5 - 5,0	
Verrucomicrobia	0,2	%	0,5 - 2,0	
Overige	0,1	%		
Enterotype				
Bacteroides				

Het menselijke microbioom kan in drie enterotypes ingedeeld worden. De darmbacteriën vormen, afhankelijk van het enterotype, stabiele, maar duidelijk verschillende clusters met typische metabolische eigenschappen. Enterotype 1 wordt gekenmerkt door hoge aantallen Bacteroides en enterotype 2 door een sterke Prevotella kolonisatie. Enterotype 3 wordt gekenmerkt door een Ruminicoccus flora.

Enterotype 1

Vaak voorkomende bacteriesoorten (TOP 6)				
Bacteroides vulgatus	1,3 x 10^11	KVE/g feces	> 6,0 x 10^10	
Faecalibacterium prausnitzii	6,3 x 10^9	KVE/g feces	> 2,0 x 10^10	
Eubacterium rectale	3,0 x 10^10	KVE/g feces	> 2,0 x 10^10	

Dr. Karin Pijper Orthomolecular-huisarts Zuiderkeerkring 448 NL-2408 RA Alphen aan den Rijn Seite 1 von 4



Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Eubacterium hallii	< 1,0 x 10^7	KVE/g feces	> 1,0 x 10^10	
Collinsella aerofaciens	< 1,0 x 10^7	KVE/g feces	> 1,5 x 10^9	
Ruminococcus bromii	< 1,0 x 10^7	KVE/g feces	> 1,0 x 10^10	
Indeling van bacteriën naar fylum met de belangrijkste bacteriegeslachten en -soorten				
Actinobacteria				
Bifidobacterium	6,0 x 10^8	KVE/g feces	> 1,0 x 10^10	
Bifidobacterium	B. longum			
Collinsella	< 1,0 x 10^7	KVE/g feces	> 2,0 x 10^9	
Collinsella aerofaciens	< 1,0 x 10^7	KVE/g feces	> 1,5 x 10^9	
Bacteroidetes				
Bacteroides	5,7 x 10^11	KVE/g feces	> 1,5 x 10^11	
Bacteroides	B. uniformis			
Prevotella	< 1,0 x 10^7	KVE/g feces	> 1,0 x 10^10	
Prevotella copri	< 1,0 x 10^7	KVE/g feces	< 2,0 x 10^10	
Alistipes spp.	1,5 x 10^10	KVE/g feces	< 3,0 x 10^10	
Firmicutes				
Butyraatproducerende bacteriën				
Faecalibacterium prausnitzii	6,3 x 10^9	KVE/g feces	> 2,0 x 10^10	
Eubacterium rectale	3,0 x 10^10	KVE/g feces	> 2,0 x 10^10	
Eubacterium hallii	< 1,0 x 10^7	KVE/g feces	> 1,0 x 10^10	
Roseburia spp.	4,4 x 10^10	KVE/g feces	> 8,0 x 10^9	
Ruminococcus spp.	4,2 x 10^10	KVE/g feces	> 1,0 x 10^10	
Totaal kiemgetal	1,2 x 10^11	KVE/g feces	> 5,8 x 10^10	
Clostridia				
Clostridium totaal kiemgetal	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^9	
Clostridien Cluster I	< 1,0 x 10^7			
Clostridium histolyticum	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Clostridium perfringens	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Clostridium sporogenes	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Overige				
Coprococcus	1,0 x 10^10	KVE/g feces	> 1,0 x 10^10	
Dialister invisus	3,0 x 10^10	KVE/g feces	< 1,5 x 10^10	
Proteobacteria				
Pathogene of potentieel pathogene bacteriën				
Haemophilus	6,3 x 10^9	KVE/g feces	< 6,0 x 10^8	
Acinetobacter	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^7	
E. coli-Biovare	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Proteus spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Klebsiella spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Enterobacter spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Serratia spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Hafnia spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Morganella spp.	< 1,0 x 10^4	KVE/g feces	< 1,0 x 10^4	
Oxalaat afbrekende bacteriën				
Oxalobacter formigenes	< 1,0 x 10^7	KVE/g feces	> 1,0 x 10^8	
Mucus-/H2S-vorming/Immunogeniciteit				
Immunogeen werkende bacteriën				
Escherichia coli	1,0 x 10^6	KVE/g feces	1,0 x 10^6 - < 1,0 x 10^8	

Case 2 Metabolic syndrome + depression

Microbiome Center

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Enterococcus spp.	1,0 x 10^8	KVE/g feces	1,0 x 10^6 - < 1,0 x 10^8	
Lactobacillus spp.	4,0 x 10^5	KVE/g feces	1,0 x 10^5 - < 1,0 x 10^8	
Mucine vorming/slijmvliesbarrière				
Akkermansia muciniphila	1,7 x 10^9	KVE/g feces	> 5,0 x 10^9	
Faecalibacterium prausnitzii	6,3 x 10^9	KVE/g feces	> 2,0 x 10^10	
H2S-vorming				
sulfaatreducerende bacteriën	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Desulfovibrio piger	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Desulfomonas pigra	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Bilophila wadsworthii	< 1,0 x 10^7	KVE/g feces	< 1,0 x 10^8	
Gisten/schimmels				
Candida albicans	< 1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida species	< 1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Geotrichum candidum	< 1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Schimmels	negatief			
Aanvullende parameters				
Vertering				
Vetgehalte	5,90	g/100g	< 3,5	
Stikstofgehalte	0,50	g/100g	< 1,0	
Suikergehalte	3,80	g/100g	< 2,5	
Watergehalte	78,20	g/100g	75 - 85	
Maldigestie				
Pancreas elastase in feces	293,17	µg/g	> 200	
Galzuren in feces	negatief		negatief	
Malabsorptie				
Calprotectine	177,03	mg/l	< 50	
Alpha-1-antitripsine	26,1	mg/dl	< 27,5	
Extra parameter(s)				
Secretoir Immunoglobuline A	6431,2	µg/ml	510 - 2040	
Extra parameter(s)				
Zonuline	52,00	ng/ml	< 55	
Speciale gastro-enterologische diagnostiek				
Gluten-sensitieve enteropathie / coeliakie				
Anti-gliadine antilichamen in feces	119,67	U/l	< 100	
Anti-transglutaminase antilichamen in feces	304,43	U/l	< 100	

Case 2 Metabolic syndrome + depression

Approach:

- Gluten-free diet
- MyOwnBlend
- Additional examination:
  - IgA tTGA: negative
  - Colonoscopy: no abnormalities

Result:

- Weight slowly decreased
- Fasting glucose 5.6, HbA1c 41
- GI complaint almost completely disappeared
- Mood normalized

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Extra parameter(s)				
Calprotectine	58,77	mg/l	< 50	119,92
Zonuline	59,26	ng/ml	< 55	67,12
Speciale gastro-enterologische diagnostiek				
Gluten-sensitieve enteropathie / coeliakie				
Anti-gliadine antilichamen in feces	43,52	U/l	< 100	119,12
Anti-transglutaminase antilichamen in feces	<50	U/l	< 100	290,12

Conclusions

Menopause is not only a hormonal transition, but a multi-system biological shift affecting metabolic, urogenital, and immune health

Declining estrogen levels drive significant changes in vaginal and gut microbiota

Vaginal microbiota: menopause leads to changes

- In reproductive age, estrogen supports a *Lactobacillus-dominated* environment
- Menopause leads to ↓ glycogen, which leads to ↓ *Lactobacillus*, which leads to ↑ pH
- Result: vaginal dysbiosis, contributing to complaints and infection risk

Gut microbiota: estrobolome affects systemic physiology

- Healthy gut microbiota regulates estrogen recycling: keeping systemic levels high
- Changes in microbiota can alter systemic estrogen exposure
- Dysbiosis leads to metabolic dysfunction, inflammation & hormonal imbalance

How to treat these changes?

- Microbiome Center's vaginal suppositories with *L. crispatus* support healthy vaginal microbiota and improves menopausal vaginal complaint
- Personalized microbiome treatment (MyOwnBlend) supports with:
  - Patient-specific health problems (e.g. mood, metabolic dysfunction, bone health, cardiovascular health, etc.)
  - Estrobolome, via deconjugation (recycling) of liver-excreted estrogen

In case of any questions contact

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Menopause: systemic changes with direct role of gut and vaginal microbiomes

Thank you for your attention